Soc. 8

THE LANCET

No. 7053 LONDON SATURDAY 1 NOVEMBER 1958 VOL. II FOR 1958

NOV 20 1958 Dont. Copy

CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

Serum-transaminase/alkaline-phosphatase Ratio in Differential Diagnosis of Jaundice
A. L. LATNER, M.R.C.P., A. J. SMITH, M.D. 915

Cardiomyotomy (Heller's Operation) for Œsophageal Achalasia
W. F. P. GAMMIE, F.R.C.S., DENYS JENNINGS, B.M., J. E. RICHARDSON, F.R.C.S. 917

Gastrointestinal Hæmorrhage and Salicylates
A. S. ALVAREZ, M.B., W. H. J. SUMMERSKILL, M.R.C.P. 920

"Salicylate Anæmia"
W. H. J. SUMMERSKILL, M.R.C.P., A. S. ALVAREZ, M.B. 925

A Skin Test in Thyroid Disease
W. WATSON BUCHANAN, F.R.F.P.S., J. R. ANDERSON, M.D., R. B. GOUDIE, M.R.C.P., KATHLEEN GRAY, B.SC. 928

Inoculation of Volunteers with J.H. Strain of New Respiratory Virus
D. A. J. TYRRELL, M.R.C.P., M. L. BYNOE, M.B. 931

Magnesium-lipid Relations in Health and in Patients with Myocardial Infarction
D. F. BROWN, M.B., R. B. MCGANDY, M.D., EDWARD GILLIE, M.D., J. T. DOYLE, M.D. 933

Phenylbutazone in the Treatment of Temporal Arteritis
S. E. BJÖRKMAN, M.D. 935

Ammonia Intoxication following Ureterosigmoidostomy
REUBEN SILBERMAN, F.R.C.S. 937

The Cardiorespiratory Syndrome of Extreme Obesity
G. M. BERLYNE, M.R.C.P. 939

PRELIMINARY COMMUNICATIONS

Plasma-hydrocortisone Levels during Cortisone Administration
I. H. MILLS, M.R.C.P., F. C. BARTTER, M.D. 941

Action of Insulin on Isolated Rat Spinal Cord
O. J. RAFAELSEN, M.D. 941

SPECIAL ARTICLES

A Hospital for the Psychotic-defective Child
GERALD O'GORMAN, M.R.C.P. 951

MEDICAL SOCIETIES

Heberden Society 943

REVIEWS

Notices of Books 944

LEADING ARTICLES

Hyaline Membrane 945
Self-medication in Tuberculosis 946

ANNOTATIONS

A Coronary Paradox 947
Wilson's Disease 948
Neonatal Myocarditis 949
Rate of Infusion 949
Lymphosarcoma in Childhood 950
Koplik's Spots 950

THE WIDDICOMBE FILE

XLIX. Benefit of Parkinson 953

PARLIAMENT

The Queen's Speech 955

LETTERS TO THE EDITOR

Future of Mental-deficiency Practice (Dr. Gordon Dutton) 956
Separatism or Reintegration? (Dr. M. H. Pappworth) 956
Mothers with Children in a Psychiatric Hospital (Dr. Thomas Stapleton) 957
Early Diagnosis of Cretinism (Dr. S. E. Keidan) 957
"False" Sickle Cells (Dr. Maurice Shapiro) 958
Local-authority Clinics (Dr. L. M. Franklin) 959
Syringe Sterilisation (Mr. H. A. Wilson, A.I.M.L.T.) 959
Crohn's Disease (Dr. J. W. Paulley) 959
"Incidence" of Hyaline Membrane in Premature Infants (Dr. Mary Avery, Dr. Margaret Drolette) 960
Ocular Lesions of Onchocerciasis (Dr. R. R. d'Haussey and others) 960
Shortage of Junior Hospital Staff (Dr. E. S. Williams) 960
Absorption of Bound Radioactive Vitamin B_{12} (Dr. A. L. Latner; Dr. Ralph Gräsbeck and others) 961
Treatment of Gonorrhœa (Dr. C. D. Alergant) 961
Severe Head Injuries (Dr. W. N. Rollason) 962
Hospital Bedding (Mr. A. F. Gray, F.C.I.S.; Mr. D. F. J. Hext-Fremlin, M.R.S.H.) 962
Carcinoma of the Cervix (Dr. H. W. Ashworth; Dr. A. A. Loeser) 962
Intra-articular Therapy in Rheumatoid Arthritis (Dr. G. E. Loxton) 963
Banting up to Date (Major D. Hamilton, M.B.) 963

PUBLIC HEALTH

Prevention and Home Care 955

IN ENGLAND NOW

A Running Commentary by Peripatetic Correspondents 955

OBITUARY

Sir John Megaw 963
Dalziel Buchanan McGrigor 964
James Andrew Gunn 965
George Sutcliffe Seed 966
Arthur Theodore Todd 966
Charles Melton Ockwell 967
Alexander Mellick 967
Hans W. Gruhle 967

NOTES AND NEWS

A Neglected Army 969

Offices: 7, Adam Street, Adelphi, London, W.C.2. *Telephone*: Temple Bar 7228/9. *Telegrams*: Lancet, Rand, London. Founded 1823. Published weekly. Registered as a Newspaper. **Price 1s. 6d.** Annual Subscription: Three guineas.

R31
L3

For non-productive cough

Tessalon Perles

Selective inhibition of the cough reflex

Tessalon has a unique mode of action as a cough depressant. It acts both by reducing the sensitivity of the pulmonary stretch receptors which form the starting point of a cough, and by depressing the transmission of afferent cough impulses.

Doses: *One 100mg. Perle (Capsule) 3 or 4 times daily swallowed whole. If necessary this dose may be doubled.*

Perles containing 100mg. nonaethyleneglycolmonomethylether-p-n-butylaminobenzoate in 25's (Basic N.H.S. price 4s. 0d.), 100's and 500's.

CIBA

'Tessalon' is a registered trade mark. Reg. user

CIBA LABORATORIES LIMITED · HORSHAM · SUSSEX

Telephone: Horsham 4321 *Telegrams: Cibalabs Horsham*

1/B

THE HOUSE OF CHURCHILL

RECENT ADVANCES IN CEREBRAL PALSY
Edited by RONALD S. ILLINGWORTH, M.D., F.R.C.P., D.P.H., D.C.H.
136 illustrations. 50s

RECENT ADVANCES IN PÆDIATRICS
New (Second) Edition. Completely changed contents. By various authors under the editorship of DOUGLAS GAIRDNER, D.M., F.R.C.P.
82 illustrations. 48s.

RECENT ADVANCES IN OTO-LARYNGOLOGY
Third Edition. By F. BOYES KORKIS, M.B., Ch.B., F.R.C.S., D.L.O.
149 illustrations. 60s.

RECENT ADVANCES IN OBSTETRICS AND GYNÆCOLOGY
Ninth Edition. By A. W. BOURNE, M.A., M.B., F.R.C.S., F.R.C.O.G., and L. H. WILLIAMS, M.D., M.S., F.R.C.S., F.R.C.O.G.
78 illustrations. 38s.

RECENT ADVANCES IN UROLOGY
By HOWARD G. HANLEY, M.D., F.R.C.S.
83 illustrations. 30s.

METABOLIC DISTURBANCES IN CLINICAL MEDICINE
Edited by G. A. SMART, B.Sc., M.D., F.R.C.P.
35 illustrations. 45s.

MEDICINE: Essentials for Practitioners and Students
By G. E. BEAUMONT, M.A., D.M., F.R.C.P., D.P.H.
Seventh Edition. 70 illustrations. 45s.

MEDICAL TREATMENT
By K. S. MacLEAN, M.A., M.D., F.R.C.P.
5 illustrations. 50s.

BIOCHEMISTRY AND THE CENTRAL NERVOUS SYSTEM
By H. McILWAIN, Ph.D., D.Sc.
New (Second) Edition. Ready this month. 45 illustrations. About 45s.

By the same author:

CHEMOTHERAPY AND THE CENTRAL NERVOUS SYSTEM
61 illustrations. 45s.

BIOCHEMICAL DISORDERS IN HUMAN DISEASE
By various authors. Edited by R. H. S. THOMPSON, M.A., D.M., and E. J. KING, M.A., Ph.D., D.Sc., F.R.I.C.
121 illustrations. 90s.

KINETICS AND THERMODYNAMICS IN BIOCHEMISTRY
By H. GEOFFREY BRAY, D.Sc., and KENNETH WHITE, B.Sc., Ph.D., A.R.I.C.
71 illustrations. 42s.

A SYNOPSIS OF HYGIENE
(Jameson and Parkinson)
By LLYWELYN ROBERTS, M.D., M.R.C.P., D.P.H., assisted by KATHLEEN M. SHAW, *M.B.E.*
New (Eleventh) Edition. 22 illustrations. 60s.

THE PRACTICE OF INDUSTRIAL MEDICINE
By T. A. LLOYD DAVIES, M.D., F.R.C.P.
Second Edition. 15 illustrations. 30s.

THE EXAMINATION OF WATERS AND WATER SUPPLIES (Thresh, Beale and Suckling)
By EDWIN WINDLE TAYLOR, M.A., M.D., M.R.C.S., D.P.H.
Seventh Edition. 51 illustrations. 100s.

Eden and Holland's MANUAL OF OBSTETRICS
By ALAN BREWS, M.D., M.S., F.R.C.S., F.R.C.O.G.
Eleventh Edition. 61 plates (12 coloured) and 371 text-figures. 63s.

THE NORMAL CHILD
Some Problems of the First Five Years and Their Treatment
By R. S. ILLINGWORTH, M.D., F.R.C.P., D.C.H.
Second Edition. 69 illustrations. 33s.

NON-TOXÆMIC HYPERTENSION IN PREGNANCY
A Symposium edited by NORMAN MORRIS, M.D., M.R.C.O.G., and J. C. McCLURE BROWNE, F.R.C.S.Ed., F.R.C.O.G.
78 illustrations. 35s.

DISORDERS OF THE BLOOD
Diagnosis, Pathology, Treatment and Technique
By Sir LIONEL WHITBY, C.V.O., M.C., M.D., F.R.C.P., D.P.H., and C. J. C. BRITTON, M.D., D.P.H.
Eighth Edition. 20 plates (12 coloured) and 125 text-figures. 75s.

CHEMICAL METHODS IN CLINICAL MEDICINE
By G. A. HARRISON, M.D., B.Ch., F.R.I.C.
Fourth Edition. 158 illustrations, including 5 colour plates. 65s.

AN INTRODUCTION TO BLOOD GROUP SEROLOGY
By KATHLEEN E. BOORMAN and BARBARA DODD, M.Sc., Ph.D.
30 illustrations. 40s.

THE EVALUATION OF DRUG TOXICITY
A Symposium edited by A. L. WALPOLE, Ph.D., B.Sc., and A. SPINKS, M.A., Ph.D., B.Sc.
58 illustrations. 25s.

HALE-WHITE'S MATERIA MEDICA, PHARMACOLOGY AND THERAPEUTICS
By A. H. DOUTHWAITE, M.D., F.R.C.P.
Thirtieth Edition. 24s.

THE ESSENTIALS OF MATERIA MEDICA, PHARMACOLOGY AND THERAPEUTICS
By R. H. MICKS, M.D., F.R.C.P.I.
Seventh Edition. 28s.

Latest from U.S.A.

RETICULAR FORMATION OF THE BRAIN
Henry Ford Hospital International Symposium
Profusely illustrated. 115s.

THE ESOPHAGUS
Medical and Surgical Management
By E. B. BENEDICT, M.D., and G. L. NARDI, M.D.
Ready shortly. 16 colour plates and 108 text-figures. 105s.

J. & A. CHURCHILL LTD., 104 GLOUCESTER PLACE, LONDON, W.1

Introducing... 'NOV-ALOCOL'

an *IMPROVED* antacid preparation

with greater acid-binding power

IN hyperacidity and peptic ulcer, the power of aluminium hydroxide to provide reliable buffering is well recognized.

In 'NOV-ALOCOL' aluminium hydroxide of improved acid-binding power is combined with magnesium hydroxide in such proportion that the mixture is neither astringent nor laxative.

'NOV-ALOCOL' provides *prompt* relief because its magnesium hydroxide content immediately acts on the excess acid already in the patient's stomach, while the buffering action of the aluminium hydroxide simultaneously provides protection against subsequent acid secretion.

'NOV-ALOCOL' is *safe*: in the dosage recommended, namely two tablets before or after meals according to the lesion, it will induce neither systemic alkalosis nor acid rebound.

Each tablet contains: Aluminium hydroxide 0.375 g.; Magnesium hydroxide 0.125 g.; Excipient and flavouring q.s.

PACKS: Bottle of 50. Dispensing Packs of 250 and 500.

N.H.S. Basic Price of 50 *Tablets is* 1/10½.

Sample and literature on request.

A. WANDER LIMITED, 42 UPPER GROSVENOR STREET, GROSVENOR SQUARE, LONDON W.1.

M398

Relief for the asthmatic child

Relief from the apprehension and acute distress of an asthmatic attack is provided by 'ENGLATE.' In almost all cases gastrointestinal disturbance is entirely absent. The combination of theophylline sodium with glycine permits full and effective therapeutic activity and by reducing gastric precipitation of theophylline enables larger doses to be prescribed.

UNIQUE BUFFERED THEOPHYLLINE SYRUP

ENGLATE

Trade Mark *Theophylline Sodium Glycinate*

SYRUP (containing 120 mg. of theophylline sodium glycinate per 4 ml.) for children up to 12 years. Available in bottles of 8 fluid ounces.

TABLETS (300 mg. of theophylline sodium glycinate). Available in bottles of 50 and 500.

Literature is available on request.

A Nicholas Product

A. & G. Nicholas LTD. *Slough, Bucks, England*

together in... CORTODERM

The Lacto-Calamine base in Cortoderm protects patients from the risk of sensitisation attributed to some vehicles by Goldsmith (*Practitioner*, 1955, **175**, 575).

CORTODERM TRADE MARK

Packings: 10g. tubes containing either 0·25%, 0·5% or 1% hydrocortisone acetate in a cream base of Lacto-Calamine.

Basic N.H.S. cost: 0·25% 3/3d. 0·5% 5/2½d. 1% 9/9d. per tube.

THE CROOKES LABORATORIES LTD · PARK ROYAL · LONDON NW10

EAR WAX *Removed this easy way*

The removal of wax from the external auditory meatus has, in the past, normally entailed attendance by the patient for diagnosis and for the prescription of a suitable loosening agent, and a second attendance a few days later for syringing.

Now, by the use of Cerumol Ear Drops, wax can be removed in most cases at one visit. A few drops of Cerumol can be instilled into the ear and, while another patient is being attended to, the soft cerumen dissolves and the harder wax disimpacts. The wax can then be removed by gentle syringing or with cotton wool. The wax may even be found to run out of the ear on its own accord, in which case patients themselves may instil Cerumol at home, obviating further attendances.

Cerumol is anti-bacterial, non-irritating and harmless to the lining of the external auditory meatus or the tympanic membrane.

Cerumol is included in Category No. 4 of the M.O.H. classified list of Proprietary Preparations and may be prescribed on N.H.S. Form E.C.10.

PACKS—*For Surgery Use*: 10 *c.c. vial—separate dropper included.* (*Basic N.H.S. price* 2/8.) *For Hospital Use*: 2 *oz. and* 10 *oz. bottles.*

CERUMOL
Regd. TRADE MARK

EAR DROPS
for the easier removal of wax

If you wish to test for yourself and have not received recently a 10 *c.c. vial, please write or telephone direct to:*

LABORATORIES FOR APPLIED BIOLOGY LTD · 91, AMHURST PARK · LONDON N.16 · Telephone: STAmford Hill 2252

MANAGEMENT OF PAIN

'DF 118'

a potent oral analgesic

In general practice 'DF 118' fills the gap between Tab. Codein. Co. and Morphine. It causes fewer side effects than other analgesics of equal potency and is not DDA.

	Pack	Basic NHS Price
Tablet of 30 mg	25	5s. 0d.
do.	100	16s. 8d.

DUNCAN FLOCKHART OF EDINBURGH

The Doctors' House

DUNCAN, FLOCKHART & CO. LTD., WHEATFIELD ROAD, EDINBURGH 11

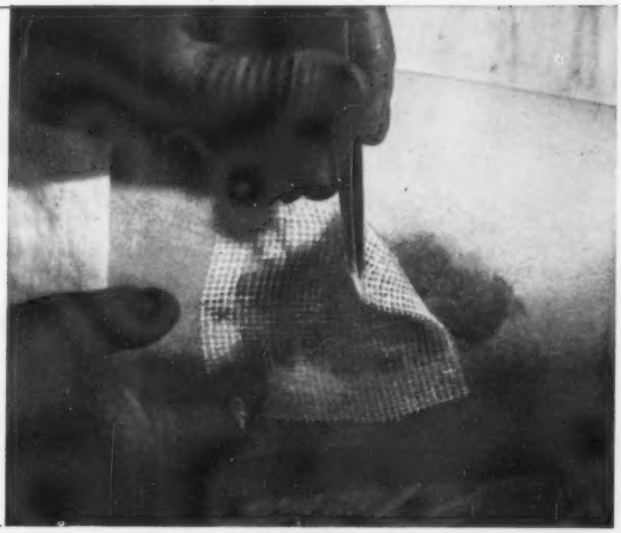
adf 251

CARBONET

TRADE MARK

A new, non-adherent dressing with these important properties

* **Water-soluble mass—painlessly removed**
* **Porous—no maceration—quicker healing**
* **Unmedicated—no sensitivity**
* **Stable and inert**
* **Easy to handle**



'Carbonet' is an open-mesh gauze dressing impregnated with a water-soluble polyethylene glycol mass. It is indicated for use on all types of open wounds and provides a non-adherent barrier between the wound surface and overlying dressings. The outstanding merit of 'Carbonet' is that it can be removed from a wound or ulcer without causing pain to the patient or trauma to epithelial and granulation tissue.

AVAILABILITY:

Sealed tins of 36 dressings—each dressing size 3¾" x 3¾" (Non-interleaved.)
Sealed tins containing a 4 yd. strip, 7½" wide, folded zig-zag. 'Carbonet' is sterilised ready for immediate use—may be re-sterilised.

CARBONET

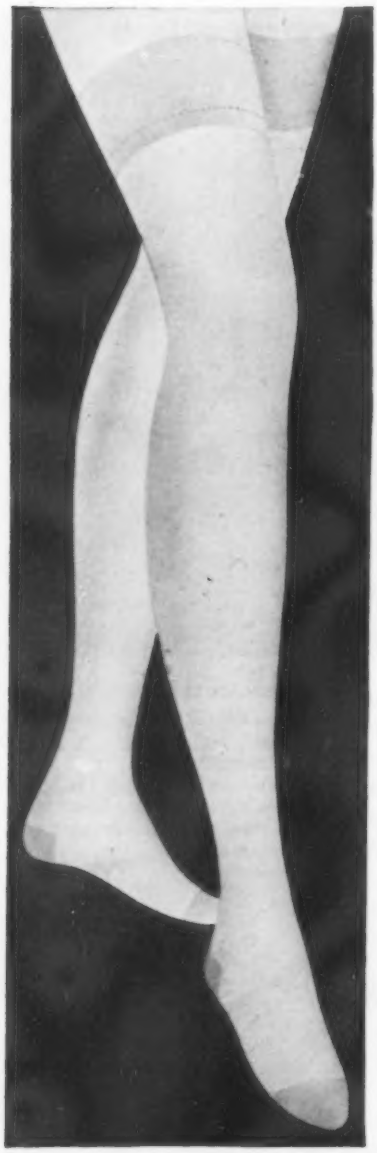
a new non-adherent dressing

S&N

DETAILS FROM SMITH & NEPHEW LTD., WELWYN GARDEN CITY, HERTS.

Now available on N.H.S.

The NEW *full-footed*



Nylastik

NYLON ELASTIC YARN
Lightweight **STOCKINGS**

For the woman patient :

SUPPORT WITH LIGHTNESS.....
FULL-FOOTED. UNDETECTED IN WEAR

The new Nylastik stockings, now available on N.H.S., give a degree of support hitherto unobtainable in any lightweight elastic yarn hosiery.

Their introduction has led to a new conception of the lightness and aesthetic appearance which can be successfully combined with efficient compression and durability.

In cases of early varices for which elastic hosiery is prescribed, Nylastik stockings are notably successful. They are particularly suitable for pre-natal wear. In many other cases, even where there is a long-standing need of surgical hosiery, the support of Nylastik may prove entirely sufficient.

The patient gains the support that you wish her to have, yet is spared the embarrassment of revealing to others that she wears elastic stockings!

Prescribable on N.H.S.

Nylastik

NYLON ELASTIC YARN
Lightweight **STOCKINGS**

THE SCHOLL MFG. CO. LTD., 182-204 ST. JOHN STREET, LONDON, E.C.1

6

AN IMPORTANT NEW APPROACH TO ORAL ANALGESIA

A **coated** tablet designed to give entirely new protection against the known side effects of Aspirin

DASCOTE

coated with Dihydroxy Aluminium Sodium Carbonate

Unlike buffered aspirin tablets in which the antacid ingredient is intimately mixed with the analgesic, 'Dascote' has a *core* of aspirin plus phenacetin *coated* with an antacid compound. Whereas with ordinary tablets granules of aspirin as well as the

antacid are free to touch the gastric mucosa, with 'Dascote' the antacid coating dissolves and reduces stomach acidity before the analgesic is released.

This is 'Dascote's' first advantage. The second advantage of 'Dascote' lies in the superior antacid used, Dihydroxy Aluminium Sodium Carbonate, an exclusive compound tested and proved to be more effective than other antacids.

PROOF OF DIHYDROXY ALUMINIUM SODIUM CARBONATE'S EFFECTIVENESS

Recent tests were conducted at the LaWall and Harrisson Research Laboratories, Philadelphia, with persons who secreted gastric juice with a high concentration of acid. Dihydroxy Aluminium Sodium Carbonate was compared with aluminium hydroxide, calcium carbonate and sodium bicarbonate. Over the test period of seventy-five minutes only Dihydroxy Aluminium Sodium Carbonate maintained the gastric pH within or close to the optimum range of pH3 to pH5.5.

Further tests have been carried out by Universal Laboratories, Folkestone, on persons given aspirin alone and aspirin in combination with Dihydroxy Aluminium Sodium Carbonate. The salicylate levels in the blood were shown to be the same between these two groups, and Dihydroxy Aluminium Sodium Carbonate neither increases the time taken for the salicylates to become traceable, nor decreases the period over which they are recoverable.

For these reasons, Universal Laboratories Limited is proud to introduce 'Dascote' to the British public, confident that 'Dascote' will fulfil a very real need in persons who require an effective analgesic particularly for those who suffer from dyspeptic conditions which render ordinary aspirin unsuitable.

DASCOTE TRADE MARK

UNIVERSAL LABORATORIES LIMITED · FOLKESTONE

The esters of NICOTINIC, SALICYLIC and p-AMINOBENZOIC acids bring relief to cases of arthritis and rheumatism

"Thank you, doctor"

IN CASES of soft-tissue rheumatism, and arthritic disorders, many doctors are tending more and more to regard Transvasin as an indispensable adjuvant to treatment.

For Transvasin is composed of the esters of nicotinic, salicylic and p-aminobenzoic acids. These esters readily pass the skin barrier in therapeutic quantities, and so enable an effective concentration of drugs to be built up where they are needed.*

Transvasin not only induces vasodilation of the skin with a superficial erythema, but also brings about a deep hyperaemia of the underlying tissues. It is non-irritant and can be safely used on delicate skins.

It is now being widely prescribed, with successful clinical results. Since a very small quantity is sufficient for each application, the cost of treatment is extremely low.

*Therapeutische Umschau 1952, 9, 143.

Tetrahydrofurfuryl salicylate	*14%*
Ethyl nicotinate	*2%*
n-Hexyl nicotinate	*2%*
Ethyl p-aminobenzoate	*2%*
Water-miscible cream base ad	*100%*

Transvasin is available in 1 oz. tubes, basic N.H.S. price in the U.K. 2/6 plus P.T., and is not advertised to the public. It may be prescribed on Form E.C.10. Samples and literature will be gladly sent on application

LLOYD-HAMOL LTD

11 WATERLOO PLACE, LONDON, S.W.1. WHITEHALL 8654/5/6

Transvasin is the registered trade mark of Lloyd-Hamol Ltd.

For happier, healthier motherhood

One factor which has contributed to the encouraging decrease of infant and maternal mortality in civilised countries is the development of modern nutritional knowledge. A preparation which is contributing to healthier and safer motherhood in this country is PREGNAVITE. This comprehensive vitamin-mineral supplement is specifically formulated to fulfil the increased daily requirements of the pregnant or lactating woman.

Packs of 60, 120 and 1,000.
Basic price to N.H.S. 1,000 tablets 32/9.

FORMULA *2 tablets, one of each colour, three times a day provide:*

liquid vitamin A conc., B.P. (40 mg.)	2,000 i.u.
liquid vitamin D conc., B.P. (30 mg.)	300 i.u.
vitamin B_{12}, B.P.	0.6 mg.
vitamin C, B.P.	20 mg.
tocoph. acet., B.P.C. (vitamin E)	1 mg.
nicotinamide B.P.	25 mg.
ferr. sulph. exsic., B.P.	204 mg.
calcium and phosphorus equivalent to 480 mg. calc. phosph., B.P.	
pot. iod., B.P.	not less than 15 p.p.m.
cupr. sulph., B.P. and mang. sulph., B.P.C.	not less than 40 p.p.m.

VITAVEL SYRUP *for children*
The delicious flavour of Vitavel Syrup solves the problem of ensuring continuity of treatment where supplementation is indicated.
Basic Price to N.H.S. 6 fl. oz. 2/6, 40 fl. oz. 16/-.

BEMAX *for all ages*
Bemax is stabilized wheat germ — the richest natural vitamin-protein-mineral supplement.

Standard Reference Cards
Factual information on all our products is available. Produced in accordance with A.B.P.I. Specifications, cards can be obtained from our representatives or from Vitamins Ltd.

(DEPT. B.3), UPPER MALL, LONDON, W.6.

VITAMINS LIMITED

GERIATRICS

The senile patient

Pacatal is particularly valuable for senile patients developing states of excitement or depression. Pacatal promotes a return to normal behaviour patterns so that the patient is easier to live with and, indeed, continues as a useful member of the family circle.

PACATAL

TRADE MARK

10-(N-methyl-3-piperidylmethyl) phenothiazine

Dosage:
1 tablet (25 mg.) two or three times a day.

Presentation:
Tablets of 25 and 100 mg. strength in bottles of 50 and 500.
Ampoules each containing 50 mg. in 2 ml. in boxes of 10 and 50.

WARNER

PAC 168/4

WILLIAM R. WARNER & CO. LTD., EASTLEIGH, HAMPSHIRE.

For radical treatment of amebiasis

By electively acting
on Entamoeba histolytica
MEBINOL definitively eliminates
the causal agent
of the disease.

« It is therefore an amebicide of undoubted value in cases of chronic intestinal amebiasis » (1)

(1) Rev. Med. Cirurg. Sao Paulo - 1958, 4, 208

MEBINOL

oxyethyl-nitrophenoxybenzyl-dichloroacetamide

- ***highly efficacious***
- ***perfectly tolerated***

CARLO ERBA MILANO

Obsolete

Gravitational Therapy

in Migraine

"You are old, Father William," the young man said,
"And your hair has become very white;
And yet you incessantly stand on your head—
Do you think, at your age, it is right?"

"In my youth," Father William replied to his son,
"I did it to cure the migraine;*
But now—why, I do it entirely for fun,
And take Cafergot when I'm in pain."

Cafergot

BY **SANDOZ**

aborts the attack of migraine in more than 80% of cases

* Standing on one's head is reputed to be a good cure for migraine[1] —but not every patient is so agile.

[1] *Brit. med. J.* (1957) 2, 633

TABLETS
1 mg. Ergotamine Tartrate B.P.
100 mg. Caffeine B.P.

SUPPOSITORIES
2 mg. Ergotamine Tartrate B.P.
100 mg. Caffeine B.P.
0.25 mg. total alkaloids of belladonna
100 mg. *iso*butylallyl barbituric acid

Sandoz House

23 Great Castle Street
London, W.1

New manufacturing technique brings significant increase in initial acid adsorption*

INTRODUCING DROXALIN GEL

Rapid adsorption of gastric hydrochloric acid is accepted as the most effective method of obtaining relief in peptic ulcer pain.

* In two minutes a single teaspoonful (3.5 mls.) of DROXALIN GEL will neutralise 50 mls. of N/10 HCl. This is *several times* the speed of acid adsorbents prepared by usual methods.

Using the well established Droxalin formulation a new and exclusive manufacturing technique has produced in DROXALIN GEL an antacid possessing this significant increase in initial acid adsorption. The advantages of quicker acting DROXALIN GEL in peptic ulcer therapy and hyperacidity will be readily recognised. The palatability of Droxalin Tablets is achieved.

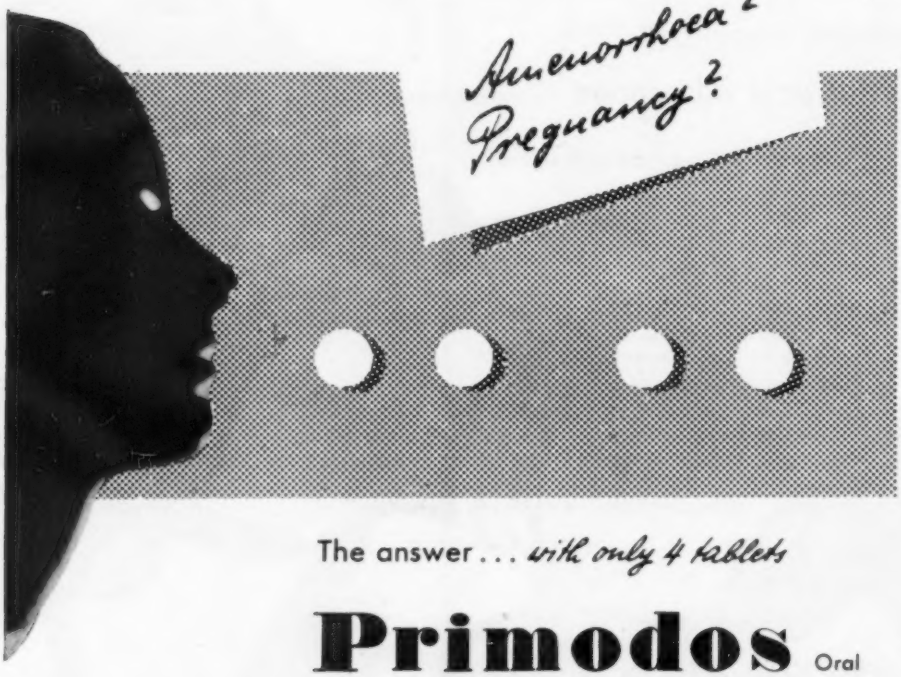
DROXALIN Gel

ACID ADSORBENT

Droxalin palatability in liquid form

ACTIVE INGREDIENTS	DOSAGE	PACKS AND PRICE
Each teaspoonful (3.5 mls.) contains 60 grains Aluminium Hydroxide Gel B.P. (equivalent to 5 grains Dried Aluminium Hydroxide Gel B.P.) and 5 grains Magnesium Trisilicate B.P.	One or two teaspoonfuls one half-hour after meals. Repeat as necessary.	DROXALIN GEL is available in 8 oz. and 80 oz. bottles. Prescribable on E.C.10. Basic N.H.S. cost. 1/10d per 6oz. bottle.

CLINICAL TRIAL SAMPLES ON REQUEST TO :— SCOTT & TURNER LTD. NEWCASTLE UPON TYNE



The answer . . . *with only 4 tablets*

Primodos Oral

containing the **new powerful** oral progestagen **Nor-ethisterone.**

The administration of 2 tablets Primodos on each of 2 consecutive days in cases of amenorrhoea of short duration causes a bleeding resembling a true menstruation after 3-6 days. If bleeding does not occur pregnancy is highly probable.

Original Packing: 4 tablets each containing 10 mg nor-ethisterone and 0,05 mg. ethinyl-oestradiol

Prescribable on N.H.S. Form E.C. 10

Samples and literature available upon request

SCHERING A.G. BERLIN

Sole distributors for the U.K. Pharmethicals (London) Ltd
20, Gerrard Street, London, W 1

Irish office: Messrs. H E Clissmann, 20, Merrion Square, Dublin

Primodos is marketed in Eire as DUOGYNON Oral

Relief of RHEUMATIC PAINS

with diethylamine salicylate

Algesal is the original skin-penetrating cream containing diethylamine salicylate. In 1955 a report of a clinical trial with Algesal appeared in the British Journal of Physical Medicine[1]. The report concluded:

"This preparation is a valuable addition to our therapeutic resources for the symptomatic relief of rheumatic pains. Clinical trial of 10% diethylamine salicylate cream *(Algesal)* showed significant relief of soft tissue rheumatic pains as compared with a dummy preparation."

Experimental work[2] has proved that diethylamine salicylate has a skin penetrative power 3 to 5 times that of other salicylates studied, and is completely non-irritating to the skin.

Over the past 5 years wide medical experience with Algesal has shown that symptomatic relief of common soft-tissue rheumatism can be achieved *without* counter-irritation, by the percutaneous route.

Algesal Balm contains the single active ingredient —10% diethylamine salicylate— in a soothing vanishing cream.

It is indicated in all the rheumatic syndromes seen in general practice: fibrositis, lumbago, osteo-arthritis, tenosynovitis, pain and stiffness after exercise.

Pads of tear-off leaflets describing special remedial exercises are available for giving to patients with lumbo-sacral strain, osteoarthritis of the knee, frozen shoulder and painful foot strain.

[1] March 1955. p.62
[2] Halpern, B., Gaudin, O., et al (1948) C. R. Soc. Biol. (Paris) **142**, 819

Algesal

percutaneous salicylate cream for the relief of rheumatic pain by inunction

Samples and full descriptive literature available on request to

E.G.H. LABS. Peru Street, Salford 3, Lancs.

Only Nulacin provides intragastric milk-alkali drip therapy for the ambulatory patient

"In view of the ineffectiveness of most of the tableted antacids, the milk-alkali tablet (Nulacin) would appear to be the antacid of choice for ambulatory therapy."

(Medical Times 1958, **1**, 74)

NULACIN TABLETS have been developed so that when allowed to dissolve slowly in the mouth, they give continuous milk-alkali drip therapy and provide a treatment of peptic ulcer and other conditions associated with hyperacidity. The effectiveness of Nulacin therapy has been established by clinical work in many countries. The following are a few references to the literature:

Antacids. *The Practitioner*, January 1957, **178:** 43

Antacids in Peptic Ulcer. *The Practitioner*, January 1956, **176:** 103

Recent Advances in the Ulcerative Diseases of the Gastrointestinal Tract. *Amer. J. Gastro.*, December 1956, **26:** 665

Ambulatory Continuous Drip Method in the Treatment of Peptic Ulcer. *Amer. J. Dig. Dis.*, March 1955, **22:** 67-71

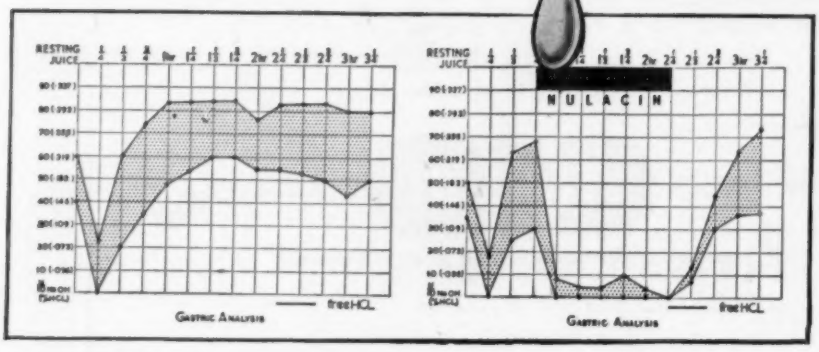
Management of Peptic Ulceration in General Practice. *Med. World*, December 1954, **81:** 591-601

Clinical Investigation into the Action of Antacids. *The Practitioner*, July 1954, **173:** 46

Further Studies on the Reduction of Gastric Acidity. *Brit. Med. J.*, 23rd January 1954, **1:** 183-184

Control of Gastric Acidity by a New Way of Antacid Administration. *J. Lab. & Clin. Med.*, 1953, **42:** 955

The Effect on Gastric Acidity of "Nulacin" Tablets. *Med. J. Aust.*, 28th November 1953, **2:** 823-824



Nulacin tablets have no B.P. equivalent and have been classified in categories 3 & 4 by the Joint Committee on Prescribing.
The basic N.H.S. price of the 25 tablet tube is 2/-.

Further information is available from:
HORLICKS LIMITED, PHARMACEUTICAL DIVISION, SLOUGH, BUCKS.

STOP

nasal congestion orally with 'Triominic'

WANDER

"timed-release" tablets

The *NEW* concept for relief of the Common Cold

In the common cold and postnasal drip, one "timed-release" 'TRIOMINIC' tablet brings welcome relief of symptoms in minutes. Running noses stop, clogged noses open—and stay open for 6 to 8 hours. The patient can breathe again.

'Triominic' is not likely to cause secondary congestion, and it eliminates local overtreatment and consequent nasal pathology, such as commonly follow the use of topical decongestants in the form of sprays and nasal drops.*

**Illinois med. J.*, 1957 *112*, 259.

Each "timed-release" 'TRIOMINIC' Tablet contains:
Phenylpropanolamine-HCl ...50 mg.
Mepyramine maleate B.P. ....25 mg.
Pheniramine maleate .....25 mg.

'Triominic' Wander is Schedule 4.

Dosage: 1 tablet in the morning, afternoon and in the evening if needed. An average prescription is 12 tablets.

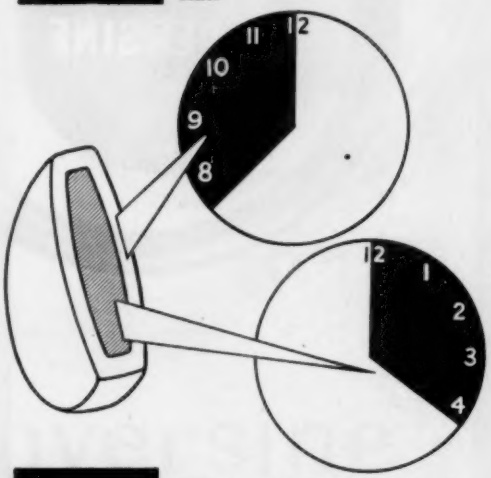
Packs: Supplied for dispensing in bottles of 50 and 250

Price: N.H.S. Basic Price for 12 tablets (4 days' treatment) is 2/3d.

Also available: 'Triominic' Syrup, for children and those adults who prefer a liquid medication, in bottles of 2 fl. oz. and 20 fl. oz. (dispensing). N.H.S. Basic Price for 2 fl. oz. is 1/10d.

Each "timed-release" tablet keeps nasal passages clear for ***6 to 8 hours****— provides "around-the-clock" freedom from congestion on just 3 tablets daily.*

FIRST the outer layer dissolves within minutes to produce 3 to 4 hours' relief



THEN the inner core disintegrates to give 3 to 4 more hours' relief

THUS 3 tablets daily 'unblock around the clock'

STOP *running noses . . .* *and open congested noses orally with 'Triominic'*

Literature and sample on signed request (S4) of physicians only M410

A. WANDER LIMITED, 42 UPPER GROSVENOR STREET, LONDON W.1.

'Inversine' and 'Saluric' introduce a New Era in the treatment of Hypertension

'INVERSINE'
(Mecamylamine Hydrochloride)

The ganglion blocking agent completely and consistently effective upon oral administrati

'SALURIC'
(Chlorothiazide)

The oral diuretic agent which also possesse hypotensive properties.

'SALURIC', already universally accepted as the only oral diuretic as effective as mersalyl, possesses the *unique* and *additional* property of *hypotensive activity*. Frequently it may be possible to control blood pressure with 'SALURIC' *alone* or with the addition of only a sedative or mild hypotensive agent. But when ganglion blocking agents are required in addition, the dosage and administration of these is greatly simplified.

LONGER LIFE FOR HYPERTENSIVES

'INVERSINE' and 'SALURIC' *concurrently*, provide: Smaller dosage of 'INVERSINE' • Smoother control of blood pressure • Freedom from, or diminution in, side-effects usually associated with ganglion blockade.

How supplied:

'INVERSINE': 10 mg. tablets (white, quarter-scored); 2.5 mg. tablets (yellow, half-scored).

'SALURIC': 0.5 G. tablets (half-scored).

'Inversine' and 'Saluric' are not supplied in a combined tablet.

'INVERSINE' and 'SALURIC' were discovered and developed in the Merck Sharp & Dohme Research Laboratories, and are manufactured in England exclusively by the Merck Sharp & Dohme Organisation. 'Inversine' and 'Saluric' are Registered Trade Marks.

Please consult literature for dosage.

Inversine
MECAMYLAMINE HYDROCHLORIDE

Saluric
CHLOROTHIAZIDE

SD **MERCK SHARP & DOHME LIMITED, HODDESDON, HERTS**

Colostomy in Ileo-Rectal Anastomosis, with interim safety valve.

Anal fistula.

Abdomino-Perineal excision of pelvic colon and rectum.

In the post-operative management of cases such as these

SIOPEL cream
TRADE MARK

is of particular value in preventing excoriation and inflammation of the skin

'SIOPEL' cream — incorporating a specially selected silicone — is smooth and easy to apply, non-irritating, non-greasy and inconspicuous.

Available in 50 G. tubes and 500 G. jars.
Basic N.H.S. cost: 2/8d. plus p. tax for a 50 gramme tube.

SIOPEL cream
TRADE MARK

Literature and further information from
IMPERIAL CHEMICAL INDUSTRIES LIMITED Pharmaceuticals Division Wilmslow Cheshire

ICI

Ph.856

an ear for CHLOROMYCETIN

Chloromycetin* Ear Drops provide a simple and certain form of local therapy for middle ear infections involving perforation, as in suppurative otitis media, chronic otorrhoea and infections of fenestration cavities. Treatment by Chloromycetin Ear Drops can be carried out successfully without constant medical supervision in contrast to the slow and tedious aural techniques of the past.

CHLOROMYCETIN EAR DROPS

speedily effective in ear infection

CHLOROMYCETIN EAR DROPS

Chloromycetin 10% in propylene glycol presented in 5 c.c. vials with dropper and in bottles of 100 c.c.

* Trade Mark

PARKE, DAVIS & COMPANY LTD. (Inc. USA)
Hounslow, Middx. Telephone Hounslow 2361

1008

Announcing

SYRUP 'V-CIL-K' Trade Mark

PAEDIATRIC

This new paediatric syrup of 'V-Cil-K' gives even the youngest patient convenient and decisive penicillin therapy. Each 5 cc. contains 125 mg. penicillin V potassium — the most effective oral penicillin yet developed. Peak levels are attained within 30 minutes, from a syrup so pleasantly flavoured that regular dosage is assured.

The dose is ¼ to 1 teaspoonful four times daily.

Available in bottles to make 30 cc. and 60 cc., each with a 5 cc. plastic spoon.

SYRUP 'V-CIL-K'

PENICILLIN V POTASSIUM

Lilly

ELI LILLY AND COMPANY LIMITED, BASINGSTOKE, ENGLAND

Lederkyn*

SULPHAMETHOXYPYRIDAZINE

*REGD. TRADEMARK

a real step forward with 'once-a-day' sulpha therapy

Full chemotherapeutic potential—antibacterial spectrum equivalent to that of sulphadiazine.

High, sustained blood levels, ensuring continuous, not intermittent, antibacterial action.

Low 'once-a-day' dosage suffices to maintain the average adult or child patient.

Lederkyn Acetyl pediatric suspension
250 mg./5cc. Bottles of 2 and 16 fl. oz.

Lederkyn tablets 0.5 gm. Bottles of 24, 100 and 500

Lederle

LEDERLE LABORATORIES DIVISION
Cyanamid OF GREAT BRITAIN LTD., London, W.C.2

CYANAMID

safe

and

effective

treatment

of

COUGH

Benylin Expectorant* is of particular value in the treatment of cough and congestion due to colds, bronchitis and allergies. It contains the anti-histamine and anti-spasmodic agent Benadryl in combination with established expectorants. A palatable raspberry-flavoured syrup; soothing, decongestant and demulcent, it readily alleviates nasal stuffiness and sneezing and is entirely suitable for children.

BENYLIN expectorant

*TRADE MARK

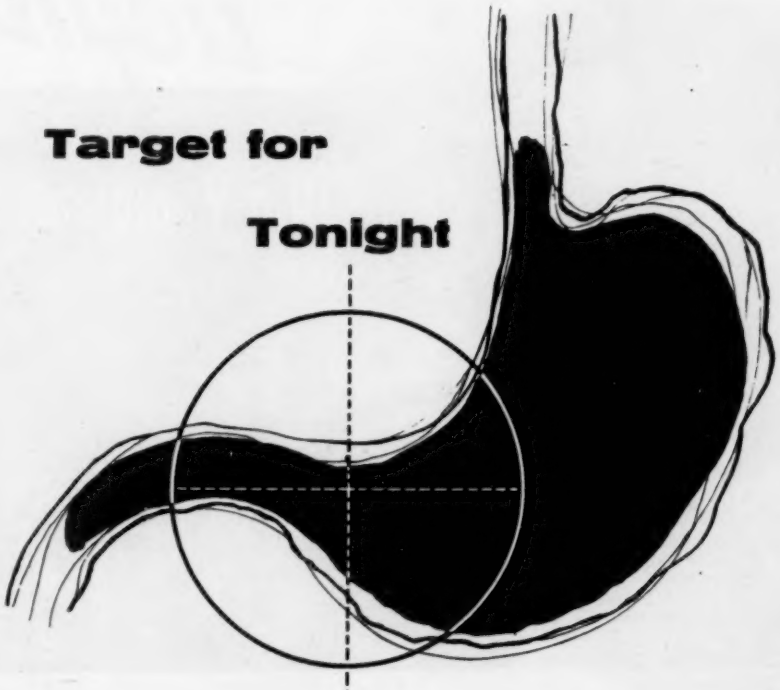
Bottles of 4, 16 and 80 fl. ounces

Parke, Davis & Co., Ltd. *(Inc. USA)*, Hounslow, Middlesex. Telephone, Hounslow 2361

1015

Target for

Tonight



Belladenal Retard

BY **SANDOZ**

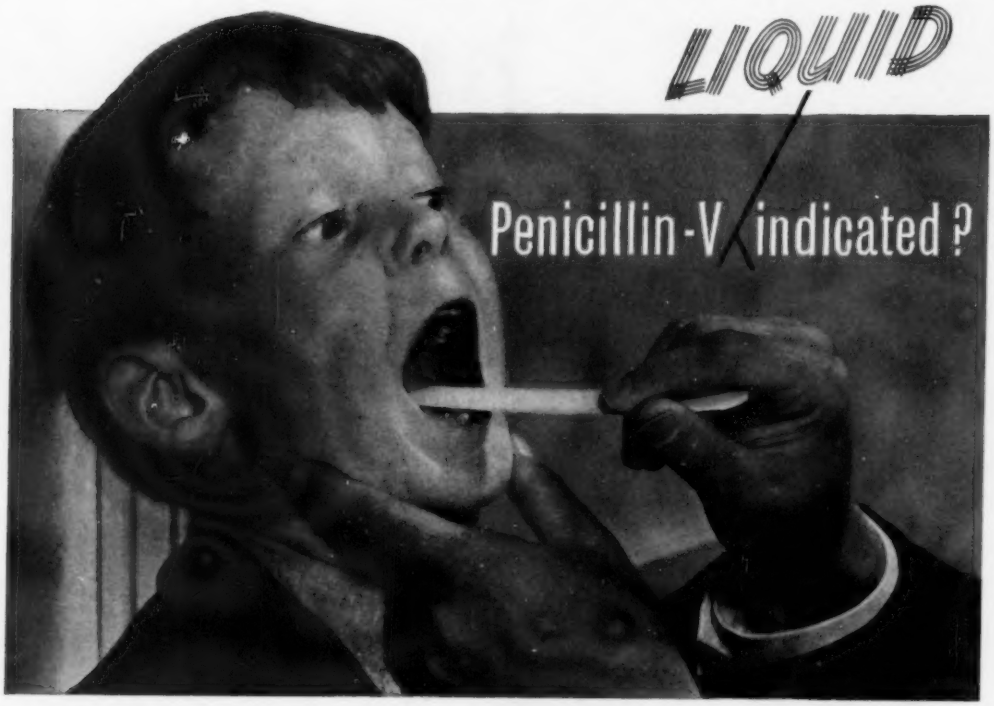
for **night** pain in peptic ulcer

TABLETS
0.25 mg. total alkaloids of belladonna
50 mg. Phenobarbitone B.P.

Sandoz Products Limited

Sandoz House
23 Great Castle Street
London, W.1

***S



Calcipen-V

SUSPENSION FORTE

WILL MEET ALL YOUR REQUIREMENTS

- A ready-prepared liquid preparation of Calcium Penicillin-V
- Stable
- Palatable
- High dosage in small volume (equals 250 mg Penicillin-V in 5 ml)
- Acceptable to children of all ages and a convenient alternative to tablets even for adults

CALCIPEN-V SUSPENSION FORTE
(Bottle of 60 ml. with plastic spoon)

Other Calcipen-V preparations
Calcipen-V Suspension (60 mg Penicillin-V per 5 ml) with plastic spoon.
Calcipen-V Tablets 60, 125 and 250 mg Penicillin-V. Containers of 20, 100, and 500.
Calcipen V-Sulpha Tablets (60 mg Penicillin-V & 0.5G. of Sulphadimidine). Containers of 20, 100, and 500 tablets.

Detailed literature gladly sent on request
BOOTS PURE DRUG COMPANY LIMITED, NOTTINGHAM, ENGLAND

When seasons change

CONTROL COUGHS

WITH

'PHENSEDYL'

trade mark brand

PROMETHAZINE COUGH LINCTUS

'Phensedyl' brand promethazine cough linctus is indicated for the relief of post-influenzal cough, or where there is bronchospasm. It is also valuable in asthmatic cough, the cough of bronchitis and the spasm of whooping-cough.

Detailed information available on request.

SUPPLIES

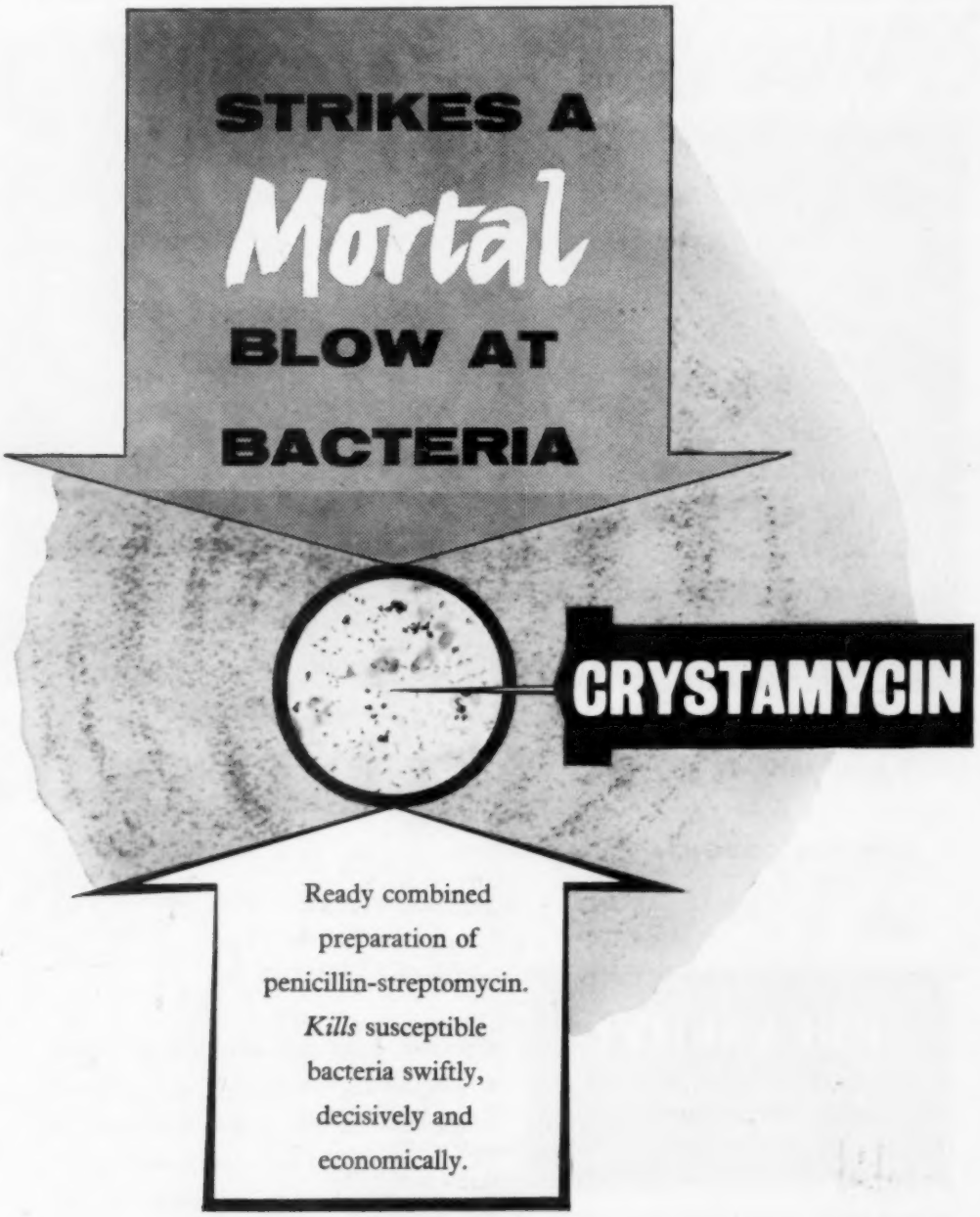
Containers of 4 fl. oz. (Each fluid drachm (3.6 c.c.) contains: Promethazine Hydrochloride B.P. 3.6 ml. Codeine Phosphate B.P. 9 mg. Ephedrine Hydrochloride B.P. 7.2 mg.)

MANUFACTURED BY

MAY & BAKER LTD

An **M&B** *brand Medical Product*

DISTRIBUTORS: PHARMACEUTICAL SPECIALITIES (MAY & BAKER LTD · DAGENHAM



A single dose contains:

500,000 units soluble sodium penicillin; 0.5 G. streptomycin (as sulphate)

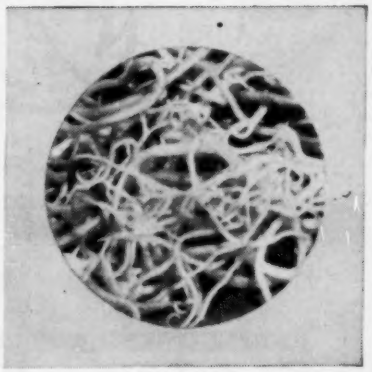
In single and five-dose vials in boxes of 10.

Glaxo Laboratories Ltd., Greenford, Middlesex BYRon 3434

Children like *it*—**worms don't**

One week's treatment with 'Antepar' Elixir or Tablets is usually sufficient to eradicate *threadworms*, a single dose to clear *roundworms*, from the gut. Effective without fasting, purging or supporting measures, 'Antepar' acts by paralysing the worms—they are then expelled by normal peristalsis.

'Antepar' Elixir is supplied in bottles of 4 fl. oz. and 20 fl. oz. It contains the equivalent of 500 mgm. of piperazine hydrate per fl. dr. 'Antepar' Tablets, for chewing, are issued in strip packs of 20 and bottles of 250. One tablet is equivalent in strength to 1 fl. dr. of Elixir.



'ANTEPAR' TRADE MARK

BURROUGHS WELLCOME & CO. *(The Wellcome Foundation Ltd.)* LONDON

Time to remember 'PERNIVIT'

TRADE MARK

for chilblains

Pernivit is effective in the treatment and subsequent prevention of chilblains. Pernivit contains nicotinic acid and vitamin K, to *improve circulation, combat arterial spasm and maintain the integrity of the blood vessel walls.*

DOSAGE

ADULTS: two to six tablets daily immediately after meals
CHILDREN: half this dosage

'PERNIVIT' tablets

Bottles of 50 at 2/-; Bottles of 500 at 11/8
Basic N.H.S. prices

Literature and specimen packings are available on request.

THE BRITISH DRUG HOUSES LTD. (Medical Department) LONDON N.1 BDH

The Lancet · Saturday 1 November 1958

SERUM-TRANSAMINASE/ALKALINE-PHOSPHATASE RATIO IN DIFFERENTIAL DIAGNOSIS OF JAUNDICE

A. L. LATNER
M.Sc. Lond., M.D. Lpool, M.R.C.P., F.R.I.C., D.I.C.
READER IN MEDICAL BIOCHEMISTRY, UNIVERSITY OF DURHAM

A. J. SMITH
M.A. Cantab., M.D. Durh.
LECTURER IN CHEMICAL PATHOLOGY, UNIVERSITY OF DURHAM

From the Department of Pathology, King's College, in the Royal Victoria Infirmary, Newcastle upon Tyne

THE levels of the serum-transaminase enzymes are sensitive indices of the presence of liver disease involving cellular necrosis. Both the serum glutamic-oxaloacetic (S.G.O.T.) and the serum glutamic-pyruvic (S.G.P.T.) transaminases have been studied (Wroblewski and La Due 1955, 1956, Pryse-Davies and Wilkinson 1958); and it has been suggested that S.G.P.T. is a more sensitive index

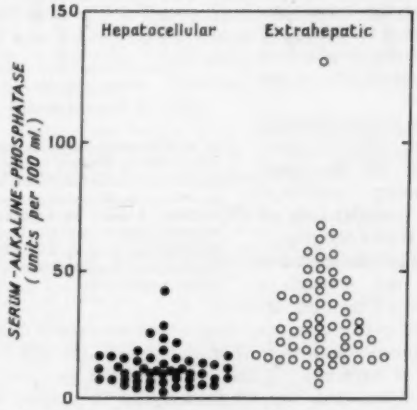


Fig. 1—Comparison of the serum-alkaline-phosphatase levels in hepatocellular jaundice and jaundice due to extrahepatic obstruction.

than S.G.O.T. (Wroblewski and La Due 1956). The S.G.P.T./S.G.O.T. ratio has been found to be inverted in the serum of patients with acute hepatocellular damage (De Ritis et al. 1957).

It has long been known that the level of serum-alkaline-phosphatase tends to rise in liver disease associated with jaundice, especially that due to extrahepatic obstruction. The level of the serum-transaminase, however, tends to be lower in jaundice due to extrahepatic obstruction. It seemed likely, therefore, that the transaminase/alkaline-phosphatase ratio might help in the diagnosis of jaundice, for in hepatocellular disease the ratio could be expected to be appreciably higher than in extrahepatic obstruction; and the investigation recorded here was designed to examine this possibility.

The usefulness of combining the serum-thymol reaction with the serum-alkaline-phosphatase test is well recognised (Maclagan 1947, Latner 1948). In this investigation, therefore, the flocculation test was also carried out to see whether it could be an additional aid in those cases in which the transaminase/alkaline-phosphatase ratio was of no great help.

Methods

Serum-transaminases were estimated by the methods of Reitman and Frankel (1957), the reagents being those supplied by the Sigma Chemical Co. This technique was chosen because the appropriate reagents are readily available to all types of laboratory and no special apparatus other than a good photoelectric colorimeter is required. We in fact used a spectrophotometer.

Plasma-alkaline-phosphatase was determined by the method of Jenner and Kay (1932).

Thymol turbidity and flocculation tests were carried out by a modification (Latner and Pendlenton 1949) of methods previously described (Maclagan 1944, 1947, Neefe 1946). Simple visual matching was carried out for the turbidity measurement. The thymol reaction was regarded as positive if the turbidity was above 4 units or the flocculation after 24 hours was 2+ or more.

Material

106 jaundiced patients, admitted to the Royal Victoria Infirmary over the period of one year, were investigated. In all the serum-bilirubin was greater than 1·6 mg. per 100 ml. Diagnosis was firmly established by liver biopsy, laparotomy, the subsequent clinical history, or necropsy. All cases of hæmolytic jaundice during this time were excluded from the series.

The group comprised 50 cases of jaundice due to hepatocellular disease (acute or chronic hepatitis) and 56 cases of jaundice with extrahepatic obstruction (gallstones, carcinoma of the head of the pancreas and of the biliary tract, metastatic carcinoma, or chronic pancreatitis).

Results

The serum-alkaline-phosphatase levels shown in fig. 1 illustrate the higher levels in jaundice due to extrahepatic obstruction. All but 1 of the cases with a serum level

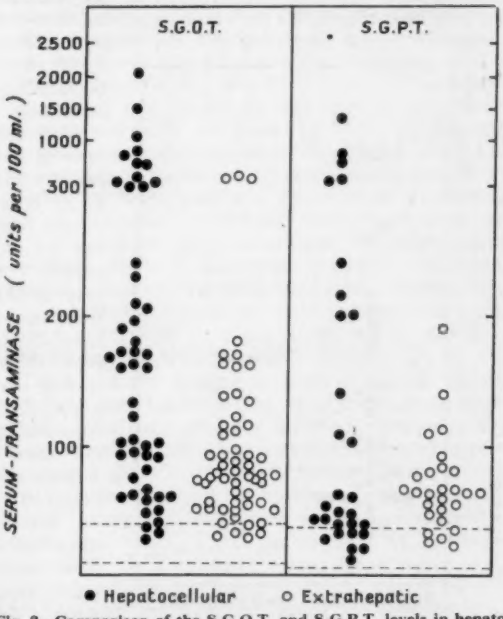


Fig. 2—Comparison of the S.G.O.T. and S.G.P.T. levels in hepatocellular jaundice and jaundice due to extrahepatic obstruction. In each case the horizontal interrupted lines indicate the range of normal values.

above 30 units belonged to this group. This is no great help in diagnosis, however, since many of the cases showed levels below 30 units. On the other hand, we have seen patients with hepatocellular jaundice who had serum levels well above this value.

The serum-transaminase levels are shown in fig. 2. The S.G.O.T. was determined in all patients, but the S.G.P.T. in only 56. Levels tended to be higher in hepatocellular disorders, in striking contrast to the alkaline-phosphatase. An unexpected finding was that this tendency was more evident with S.G.O.T. than with S.G.P.T., in contrast to the findings of other workers (Wroblewski and La Due 1956). Because of this, our further remarks will be concerned with S.G.O.T. and not with S.G.P.T.

In fig. 3, the transaminase/alkaline-phosphatase ratios show that the differences between extrahepatic obstruction and hepatocellular disease are now very much greater. Nearly three-quarters of the cases with hepatocellular disease had a ratio of 7 or above. Only 4 of the cases with extra hepatic obstruction had similar ratios. On the other hand, more than half the extrahepatic group had ratios of 3 or below, whereas in no single case with hepatocellular disease was a similar figure found.

Discussion

It can thus be assumed that when the S.G.O.T./alkaline-phosphatase ratio is above 7 in the presence of jaundice, the chances are quite strong that the patient is suffering from hepatocellular disease. Only 4 cases in the group with extrahepatic obstruction had values above this level. They included 2 cases of metastatic carcinoma, a biliary cirrhosis, and an empyema of the gallbladder. The unusual behaviour was of no great consequence in the patients with metastases but would have been misleading if the clinical diagnosis had been obscure in the patient with empyema of the gallbladder. The intense toxæmia may have been responsible for a ratio suggesting liver-cell damage. It is not surprising that the biliary cirrhosis appeared as hepatocellular disease.

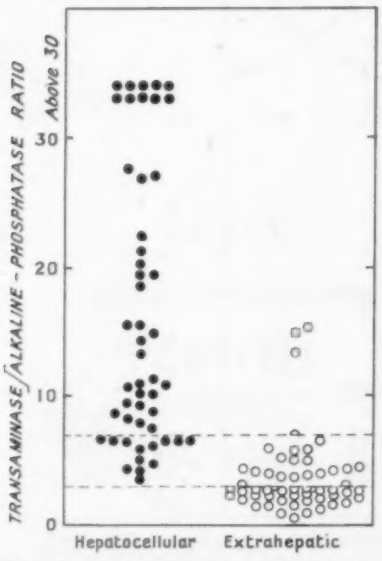


Fig. 3—Transaminase/alkaline-phosphatase ratios in hepatocellular jaundice and jaundice due to extrahepatic obstruction. The horizontal interrupted lines indicate the range of values of 3 to 7.

When the ratio is between 3 and 7, no diagnostic help can be expected. The cases giving these values have, however, been further analysed by considering the thymol responses in relation to the serum-alkaline-phosphatase levels (Maclagan 1947) as interpreted by Latner (1948). All thymol-positive cases can be regarded as due to hepato cellular disease. With a negative thymol reaction, patients with extrahepatic jaundice tend to have an alkaline-phosphatase of 18 units or above, and those with hepatocellular jaundice tend to fall at 12 units or below. Analysis of the whole group in this way shows that diagnosis would have been correct in 82 cases, or 77% of the series; there would have been diagnostic error in 6 cases, or approximately 6% of the series; an equivocal result would have been obtained in 18 cases or 17% of the series.

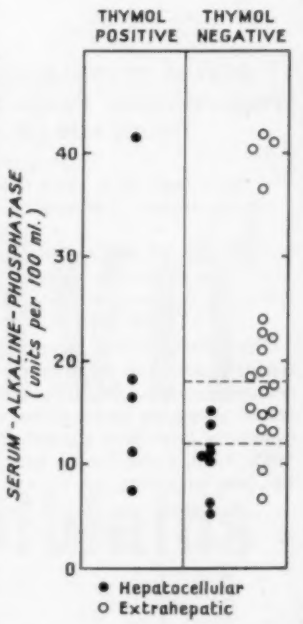


Fig. 4—The serum-alkaline-phosphatase levels in relation to the thymol reaction in those cases with a transaminase/alkaline-phosphatase ratio between 3 and 7 in hepatocellular jaundice and jaundice due to extrahepatic obstruction. The horizontal interrupted lines indicate 12 and 18 units respectively.

The results obtained by applying this procedure to the cases remaining equivocal after consideration of the transaminase/alkaline-phosphatase ratio are shown in fig. 4. They are arranged in two columns, those which were thymol positive and those which were thymol negative. It will be seen that, as expected, all the cases giving a positive serum thymol reaction were hepatocellular in origin; with a negative thymol reaction, those cases with serum-alkaline-phosphatase levels above 18 units were due to extrahepatic obstruction. There were 8 thymol-negative cases with phosphatase levels of 12 units or below. Of these, 6 were hepatocellular in origin and 2 were due to extrahepatic causes. In both the latter, however, the obstruction was due to carcinoma; extensive carcinoma of the common bile-duct and metastases from carcinoma of the stomach. Here again, had one decided that these 2 cases were suffering from hepatocellular disorder not very much harm would have been done.

On the other hand, there were still 9 thymol-negative cases with alkaline-phosphatase levels between 12 and 18 units, in which a firm diagnosis could not be made on the laboratory tests alone.

It will thus be seen that by using the transaminase/alkaline-phosphatase ratio and by re-examining equivocal cases falling between the levels of 3 and 7 by the additional help given by consideration of the serum thymol reaction tests, it would have been possible to obtain a correct diagnosis in 48 out of the 50 cases of hepatocellular jaundice. The remaining 2 cases in this group would have been in the range where diagnosis is equivocal. With extrahepatic obstructive jaundice there would have been 43 correct diagnoses, 6 diagnostic errors, and 7 in the equivocal range. Of the diagnostic errors, 4 were suffering

from carcinoma of one kind or another, 1 had biliary cirrhosis, and 1 had an empyema of the gallbladder.

In the total series of 106 cases, a correct diagnosis would, therefore, have been made in 91 instances on the laboratory investigations alone, giving a diagnostic accuracy of 86%. Diagnostic error would have occurred in 6 cases or 6%; 4 were patients with carcinoma. On the basis of the criteria used, the diagnosis would have remained equivocal in 9 cases or 8% of the series. This is better than the diagnostic accuracy obtained by considering the combination of the alkaline-phosphatase and the flocculation reaction in the whole group. We should, therefore, like to suggest the use, in the way we have described, of the combination of these three tests in the differential diagnosis of jaundice.

Summary

A study has been made of the usefulness of the combined determinations of the serum-alkaline-phosphatase, serum-transaminase, and serum-thymol reaction in the differentiation of hepatocellular jaundice from extrahepatic jaundice. Particular consideration has been given to the transaminase/alkaline-phosphatase ratio.

In a series of 106 cases, consideration of the findings would have led to a correct diagnosis in 86% of the series. The diagnostic error would have been 6%. On the basis of the criteria used, diagnosis would have remained equivocal in 8% of the series.

The results are better than those obtained by consideration of the combination of the serum-alkaline phosphatase and thymol flocculation tests.

REFERENCES

De Ritis, F., Coltorti, M. V., Guisiti, G. (1957) *Clin. chim. acta*, **2**, 20.
Jenner, H. D., Kay, H. D. (1932) *Brit. J. exp. Path.* **13**, 22.
Latner, A. L. (1948) Flocculation Reactions and Hepatic Dysfunction. M.D. Thesis, University of Liverpool.
— Pendlenton, G. B. (1949) *Biochem. J.* **44**, xxxiii.
Maclagan, N. F. (1944) *Brit. J. exp. Path.* **25**, 234.
— (1947) *Brit. med. J.* ii, 197.
Neefe, J. R. (1946) *Gastroenterology*, **7**, 1.
Pryse-Davies, J., Wilkinson, J. H. (1958) *Lancet*, i, 1249.
Reitman, S., Frankel, S. (1957) *Amer. J. clin. Path.* **28**, 56.
Wroblewski, F., La Due, J. S. (1955) *J. Amer. med. Ass.* **160**, 1130.
— — (1956) *Proc. Soc. exp. Biol., N.Y.* **91**, 569.

CARDIOMYOTOMY (HELLER'S OPERATION) FOR ŒSOPHAGEAL ACHALASIA

W. F. P. GAMMIE
B.M. Oxon., F.R.C.S.
FIRST ASSISTANT, SURGICAL UNIT

DENYS JENNINGS
B.M. Oxon., D.M.R.E.
RESEARCH FELLOW IN GASTROENTEROLOGY

J. E. RICHARDSON
M.S. Lond., F.R.C.S.
SURGEON

THE LONDON HOSPITAL, LONDON, E.1

AT the International Congress of Gastroenterology (1956) in London two years ago, there was some doubt about the place of Heller's operation.

The criticism of the operation is that the circular muscle at the lower end of the œsophagus is the functional sphincter preventing reflux of gastric contents; the operation may completely destroy this sphincter or it may fail to do so. If it is not destroyed, dilatation with retention will persist; if it is destroyed, reflux of acid will lead to peptic œsophagitis and the operation will be no safer than cardioplasty (Barrett and Franklin 1949). Persistent heartburn has in fact been reported by Acheson and Hadley (1958).

Our experience, on the other hand, had left us with an impression of almost uniformly excellent results, and we decided to re-examine our cases critically to see whether the results were really as good as we thought. Some patients have some residual symptoms, and others, though symptom-free, have persistent dilatation of the œsophagus with some retention; but there is no evidence that these faults are related to the presence or absence of a functioning sphincter. On the contrary, our results suggest that it is the stage in the disease at which the operation is done that controls the final result.

Material

18 consecutive cases were reviewed. Most of these patients had been seen and operated on within a few years of onset; they were all under one surgeon, and were examined at some stage by one radiologist. The patients were followed up for at least two years, and the results were checked independently by one of us (W. F. P. G.) to avoid the fallacy of the polite patient who dislikes complaining to a surgeon who has treated him.

Results

The salient facts are shown in table I. It is meaningless to calculate an average age of onset as is done in some series. Some patients give a convincing history of ability to swallow beer or solids quicker than their friends up to some more or less clearly remembered date, and the onset of the œsophageal dilatation may also be known to within a few months from serial X-ray studies. Other patients (such as cases 4, 5, and 9) say that they have swallowed slowly since childhood, and only after operation have realised that they never swallowed normally before. The onset of achalasia can be at any time from youth to old age, and there is little convincing evidence in published reports that it is commoner in any particular decade.

We have attempted to separate the patients' estimate of the success of operation from our estimate. Difficulty arises when swallowing is described as completely normal compared with what it was before operation, but the patient continues to eat soft foods because she prefers them and to eat slowly because she always has done so. There is a further difficulty from associated indigestion. The patient may regard the operation as successful if before operation she was blown up with wind and could not swallow and after operation still gets full of wind but can swallow. If the patient (1) eats anything without discomfort, (2) keeps pace with others at meals, (3) never has any episodes of difficulty with swallowing, and (4) never gets any reflux of acid into the œsophagus, we regard the result as completely successful. In table I anything less than completely successful is marked down according to the number of these symptoms and their severity by means of a percentage which affords an arbitrary method of comparison.

There is doubt whether achalasia is a single disease, and there may be differences in different parts of the world. The most generally accepted explanation is a toxic, infective, senile, or nutritional degeneration of Auerbach's plexus in the body of the œsophagus; possibly some cases are congenital and analogous to Hirschsprung's disease. Nutritional factors have mainly been stressed by Spanish and South American writers. An alternative theory is that the histological changes are secondary to the œsophagitis which results from the stagnation of retained food, and that psychological factors are responsible for the initial breakdown.

Table II summarises some negative findings which deserve mention. The absence of any history of prolonged

TABLE I—NOTE ON 18 CONSECUTIVE CASES

Case no.	Sex	Year of birth	Age at onset (yr)	Length of history when first seen	Further delay to cardio-myotomy	Year of operation (A = abdominal T = thoracic)	Length of postoperative follow-up	Pain		Reflux or heartburn†		Patient's estimate of success (%)‡	Clinical estimate of success (%)‡
								Before op.	After op.	Before op.	After op.		
1	F	1901	42	3 yr.	30 mos	1949 (T)	8 yr.	+	+	+	+	90	90
2	F	1920	28	8 mos	14 mos	1950 (A)	7 yr.	+ +	−	±	−	100	70
3	F	1887	59	4 yr.	2 wks	1950 (T)	7 yr.	+	−	±	−	100	100
4	F	1914	38	6 mos	1 mo.	1952 (T)	6 yr.	±	−	−	−	100	100
5	F	1921	29	2 yr.	1 yr.	1953 (T)	4 yr.	+	+	+	+	90	90
6	F	1875	74	6 mos	5½ yr.•	1954 (T)	2 mos, died	+	Died	+	Died	—	—
7	F	1887	52	4 mos	15 yr.•	1954 (T)	3 yr.	+	−	−	−	100	100
8	F	1910	44	6 mos	8 mos	1954 (T)	3 yr.	−	−	+	−	90	90
9	F	1927	25	4 mos	3 yr.	1955 (A)	3 yr	+	+	+	+	60	50
10	F	1888	65	2 yr.	2 wks	1955 (T)	3 yr.	−	−	+	−	70	70
11	F	1930	20	2 yr.	3 yr.	1956 (T)	2 yr.	−	−	+	−	100	100
12	F	1888	60	3 yr.	5 yr.	1956 (A)	2 yr.	+	−	+	−	100	70
13	M	1886	63	2 mos	6 mos	1949 (T)	8 yr., died	−	−	+	−	90	70
14	M	1926	22	18 mos	7 mos	1949 (T)	8 yr.	+	+	−	−	90	90
15	M	1888	60	2 mos	2 yr.	1951 (T)	3 yr., died	−	−	±	−	100?	100?
16	M	1914	34	3 yr.	16 mos	1952 (T)	5 yr.	−	−	+	−	100	100
17	M	1902	50	20 mos	2 mos	1954 (T)	3 yr.	+ +	+	−	+	Failure	Failure
18	M	1919	34	15 mos	5 mos	1955 (T)	3 yr.	+	−	+	−	100	90

• Not continuous attendance, + = present, − = absent, ± = doubtful.
† Discomfort classified as heartburn if associated with reflux into the pharynx.
‡ See text.
?=Died of hypertensive heart-failure in a mental hospital. No mention of dysphagia in any notes, but was not specifically questioned.

diarrhœa, abuse of aperients, or alcoholic excess suggests that nutritional factors were unimportant in this series. 5 women and 2 men were overweight and still gaining when the first symptoms developed.

In cases 1, 2, 3, 6, 8, 9, and 10, either the history or the X-ray findings led to a suspicion at one stage of peptic œsophagitis. In none of the operated cases has there been any evidence of a preceding benign stricture—i.e., our experience so far fails to support the hypothesis that degeneration of Auerbach's plexus and the characteristic absence of peristalsis results from stagnation œsophagitis due to a stricture.

Operative Details

All operations and observations have been carried out on patients under general anæsthesia and with muscle relaxants.

A Ryle's tube is passed into the œsophagus, which is emptied as completely as possible before operation. In most cases the lower part of the œsophagus has been approached by a trans-thoracic incision, and in a few by an abdominal incision. The thoracic approach is always used if there is any possibility of a carcinoma and whenever the X-ray shows a long segment of narrowing in the lower œsophagus.

TABLE II—NEGATIVE FINDINGS

Case	Weight (lb.)			Effect of stress	Tobacco	Alcohol	Abuse of aperients	Diarrhœa	Teeth	Menstruation	General health	Hb (%)•	Blood-group
	At onset, as stated by patient	Lowest known before op.	Highest known after op.										
1	203	161	192	−	±	±	−	O	A	N	A	85	O+
2	100	122	133	−	±	±	−	O	A	N	G	85	A+
3	?	98	140	−	O	±	−	O	D	O	A	92	A+
4	114	99	114	−	+	O	−	O	G	N	G	90	A+
5	108	117	128	±	O	O	+	O	D	N	A	47	?
6	182	152	died	−	O	O	−	O	D	O	P	?	O+
7	?	88	125	−	O	O	−	O	D	O	A	103	A+
8	163	134	190	−	O	O	±	O	A	N	A	90	O+
9	168	103	130	−	O	O	−	O	A	N	A	67	A+
10	158	126	168	−	O	O	−	O	D	O	A	86	B+
11	157	128	168	−	±	±	−	O	A	O	A	78	O+
12	?	68	77	−	±	±	+	O	D	O	A	83	A+
13	128	104	140	+	+	+	−	O	?	..	A	97	A+
14	182	?	170	−	+	±	−	O	G	..	A	93	A+
15	125	111	132	+	+	+ +	−	O	D	..	A	?	?
16	?	126	150	−	+ +	+	−	O	D	..	A	98	O+
17	210	168	140	+	+ +	O	±	O	A	..	A	102	O+
18	?	126	152	±	+	O	−	O	A	..	A	?	B+

• 100% = 14·8 g. Hb per 100 ml.
?=not recorded. G=good. A=average. P=poor. O=absent. D=dentures. + =possibly important. − =believed to be unimportant. ± =doubtful importance. N=normal.

The crus is not divided. The œsophagus can easily be pulled up into the chest after division of the pleura. In an abdominal approach it can equally easily be pulled downwards after division of the peritoneum. The length of the incision into the muscular layer of the œsophagus has varied according to the X-ray appearance. It is always extended down to the stomach and up to a point which is thought to be well above the narrow segment. When the stomach is divided there is always bleeding which makes observation difficult. The incision is therefore started over the œsophagus and carried down to the stomach. The muscular coat of the œsophagus appears a little thicker than normal. Sometimes in dividing the muscular layer or submucous layers small nerves or blood-vessels are seen, but there does not appear to be any consistent pattern in their arrangement. The submucous layer is always well defined; and when the muscle is cut it retracts quite easily, leaving the mucosa bulging into the cut muscular layer.

There have been no operation deaths in this series, but 2 patients have had unfortunate sequelæ.

1 (case 14) had a transthoracic cardiomyotomy with an abdominal exploration through an incision in the dome of the diaphragm—i.e., not involving the crus. This incision subsequently broke down and led to a traumatic hiatal hernia, which does not however cause sufficient trouble to justify operation. He has occasional uncomfortable feelings in the chest, and these seem to occur when the splenic flexure is full of gas and pushes up into the hernial sac.

The second complication occurred in case 17 and was more serious.

Postoperative distension led to a sliding hernia of the upper pole of the stomach into the chest. Because of dullness at the base of the lung the chest was aspirated, in the course of which the stomach was entered. A localised infection followed, and this led to the gastro-œsophageal junction being fixed in the chest by adhesions in such a way that the normal valve formed by the oblique entry of the œsophagus into the stomach was abolished. Radiography shows that the cardia is completely incompetent. The patient has episodes of uncontrollable acid reflux, and recently, three and a half years after operation, an episode of severe substernal pain was followed by a sharp hæmorrhage.

In the collected series of 31 cases reported by Acheson and Hadley (1958) 7 patients required further surgical treatment to dilate the lower end of the œsophagus, and 13 out of 21 successful operations were followed by heartburn. Presumably similar experience led Wangensteen (1957) to advocate a complex procedure which involves a balloon into the œsophagus through a gastrostomy, and then cutting the circular muscle over the

TABLE III—X-RAY APPEARANCES BEFORE AND AFTER OPERATION

	Little or no œsophageal enlargement or retention			Some œsophageal enlargement and retention	Considerable œsophageal enlargement
	Little or no delay in barium swallow	Pronounced delay in barium swallow			
	Œsophageal motility almost normal	Abnormal or exaggerated œsophageal contractions		Minimal œsophageal contractions (passive œsophagus)	
Barium swallow:					
First	3• 5• 18•	1 6 13 15	8 9 17•	7 10• 14 16	2 4 11 12
Preoperative			8 15 17	5 13	14 18	1 2 3 4 6 7 9 10 11 12 16
Postoperative	1 4 11† 14 16 18	2 5 13 17	9	10	3 7	12

The numerals are case numbers.
• X-rayed at another hospital.
† Considerable dilatation when supine.
Case 8 has had no postoperative barium swallow. Cases 6 and 15 are dead.

stretched balloon. The operation is completed with a pyloroplasty. In our experience the plane of cleavage between muscle and mucosa has always been definite and no adventitious aids have seemed desirable. Recently, however, we have had a failure. A patient operated on in mid-1957 (too late to be included in this series) had a recurrence of dysphagia within three weeks. He has improved after dilatation with a Negus bag but still feels that his swallowing, though "much easier than before operation, is by no means normal". The improved results obtained by Malm (1956) by increasing the length of the incision suggest that the fault in this case was probably not failure to make the incision deep enough, but failure to divide the circular muscle over a sufficiently long segment.

Radiological Findings

Table III attempts to schematise the varying X-ray appearances before and after operation. It is difficult to do this because no two cases are quite alike. Patterns of motility change from minute to minute and from week to week. The so-called "corkscrew" appearance may be so momentary that it is difficult to time the X-ray exposure to show it, or it may persist for minutes at a time. Contraction of the lower segment may be so transient as to appear within normal limits, or so persistent as to mimic an organic stenosis. The whole œsophageal vestibule may fail to relax, or it may form a small bell or cone at the lower end of the dilated œsophagus with the final hold-up apparently localised sharply to the gastro-œsophageal junction. Sometimes the appearances suggest scleroderma; the œsophagus is passive, but there is no dilatation, and the abnormality only becomes obvious when the patient is tilted into the horizontal position. Passivity is only relative; the most dilated and passive œsophagus shows shallow ripples of contour at times. Rarely, motility seems merely an exaggeration of the normal and a silent neoplasm of the stomach invading the cardia is suspected.

The word "retention" means the presence of food remnants or appreciable amounts of fluid in the œsophagus when barium is first swallowed. Dilatation is difficult to measure satisfactorily from old X-ray films. In any patient who drinks rapidly, the œsophagus temporarily dilates; and this transient effect is exaggerated in achalasia. Thus a misleading impression may be obtained if the exposure is made while the patient is actually drinking. Sometimes there is little delay or dilatation at first, but after the patient has been examined in the head-downward position, the œsophageal muscle seems to tire rapidly. For what it is worth, table III summarises our experience of patients getting worse before operation and recovering afterwards. Our results agree with those of Acheson and Hadley (1957).

Discussion

Discomfort on swallowing interferes with the enjoyment of life more than is commonly realised. As long as there is no vomiting or serious loss of weight, patients adapt themselves to their disability; but we do them a disservice if we allow this to happen. Dilatation of the cardia with a hydrostatic bag will relieve serious obstruction sometimes for years, but it is rarely followed by the surprised and enthusiastic gratitude which seems to be the rule after cardiomyotomy; and serial X-rays confirm that after dilatation, in the absence of any complaints from the patient, the œsophagus may continue to enlarge. In none of this series, on the other hand, has further enlargement occurred after cardiomyotomy; in most cases there has been some recovery of œsophageal tone, which has continued over the years.

Our experience suggests that there are three stages.

In the *first stage* there is a discrepancy between the patient's story and what is seen on the X-ray screen. Sometimes the X-ray findings are incidental; œsophageal contractions are completely irregular and form bizarre patterns, but there is no clinical history of dysphagia and the barium meal is requested for an unrelated complaint such as diarrhœa or a longstanding ulcer. More often the reverse happens; there is a story of repeated episodes of difficulty in swallowing, usually precipitated by stress, but the X-ray changes are so slight that an inexperienced radiologist may miss them completely. Occasionally, patient, clinician, and radiologist all fail to realise that food is sticking, and the discomfort in the chest is ascribed to "indigestion". As neither fluid barium sulphate nor paste is retained in the œsophagus at this stage, and there is usually no discomfort during the examination, what happens at home during meals must be in some way different from anything the radiologist sees. The patient often attributes the difference to nervous tension or self-consciousness.

In the *second stage*, difficulty and discomfort recur at every mealtime; the œsophagus begins to enlarge, and there is some delay in the barium swallow. Characteristically the first mouthfuls of barium pass into the stomach; and then the œsophageal muscle begins to "tire" and stretch, and the barium is retained. At first these changes are reversible, and a return to the earlier stage can occur either spontaneously with an improvement in mental or physical health, or as a result of dilatation of the cardia.

In the *third stage*, the œsophagus is dilated and elongated; there is considerable retention of food, and if any contractions occur they are only shallow ripples. If this stage is allowed to persist, the changes become irreversible. At least we believe so. Occasionally this last stage is reached with slight preceding discomfort, and the diagnosis is first made from a routine chest X-ray which shows a characteristic large mottled mediastinal shadow. Some patients with a short history of dysphagia are already in this last stage when first investigated.

Olsen and Creamer (1957), who seem to have seen cases mainly in the first stage or in the third stage, describe

two different diseases under the name of " diffuse spasm " and " true achalasia ", though they admit that transitional cases occur. In our experience, transitional cases have been so common that it is simpler, at present, to think in terms of " stages ".

When cardiomyotomy is done in the second stage, the result as judged by the radiologist is good, and there may even be enough recovery of œsophageal function to permit swallowing against gravity in the Trendelenburg position; but with the recovery of tone, irregular contractions also reappear and subjective results tend to be less good. In fact the patient goes back to stage one, except that the difficulty in swallowing is now never so serious; reflux may recur, and there is a substernal sensation which is described as heartburn.

If cardiomyotomy is done late in the third stage, subjective results are excellent; but considerable retention persists, and radiographically there is little change in the appearance of the œsophagus except that barium now passes into the stomach with a lower head of pressure.

Bad clinical results are seen after making too short an incision (Malm 1956) or after operating on cases of " diffuse spasm " (Olsen and Creamer 1957)—i.e., after operating too soon. The ideal policy is to wait until there is definite dilatation and retention with a short inactive distal segment. There is no evidence that cardiomyotomy destroys an important sphincter. Heartburn after a short incision, or in patients with a persistently overactive œsophagus, is not due to gastroœsophageal reflux, but to retained food being moved to and fro. Of course, if a patient insists on living on milky foods with excessive sugar, and sucks laxative alkaline tablets, the colon will be blown up with gas, and voluntary attempts at belching will lead to acid reflux, just as they do in anyone else with this form of indigestion.

Careful study of the lives of our patients failed to reveal any environmental or psychological factors leading to the initial development of achalasia. This is too small a series on which to base any final conclusions: and different factors may be important in other parts of the world.

Summary

A consecutive personal series of 18 patients with achalasia observed for two to nine years, and followed up after cardiomyotomy for two to eight years, is reported.

If the œsophagus is enlarged and food is retained, cardiomyotomy gives better results than hydrostatic dilatation of the cardia. Postoperative radiographic studies suggest that results are better if operation is done early.

There is some evidence that operation can be done too early, and that it should not be attempted until the œsophagus is enlarged.

Cardiomyotomy by itself does not lead to incompetence of the cardia or to gastroœsophageal reflux.

We wish to thank the physicians of the hospital who referred cases to us, and Prof. Clifford Wilson and Prof. V. W. Dix for their advice in the preparation of this paper.

REFERENCES

Acheson, E. D., Hadley, G. D. (1958), *Brit. med. J.* i, 549.
Barrett, N. R., Franklin, R. H. (1949) *Brit. J. Surg.* **37**, 194.
International Congress of Gastroenterology (1956) *Gastroenterologia, Basle*, **86**, 135.
Malm, A. (1956) *ibid.* p. 208.
Olsen, A. M., Creamer, B. (1957) *Thorax*, **12**, 279.
Wangensteen, O. H. (1957) *Surg. Gynec. Obstet.* **105**, 339.

GASTROINTESTINAL HÆMORRHAGE AND SALICYLATES

A. S. ALVAREZ
M.B. Birm.
HOUSE-PHYSICIAN

W. H. J. SUMMERSKILL
M.A., D.M. Oxon., M.R.C.P.
SENIOR REGISTRAR

DEPARTMENT OF GASTROENTEROLOGY,
CENTRAL MIDDLESEX HOSPITAL, LONDON, N.W.10

MASSIVE gastrointestinal bleeding was related to salicylate consumption in one patient by Douthwaite (1938); and small series of cases were subsequently reported by Hurst and Lintott (1939), Richmond (1950), and Kelly (1956). Hurst (1943) and Avery Jones (1952) agreed that aspirin might sometimes cause hæmatemesis and melæna, and a third of 166 patients studied by Muir and Cossar (1955) had taken salicylate compounds within six hours of bleeding. Similarly, Brown and Mitchell (1956), studying the American Negro, found that 19 of 46 patients with duodenal ulceration had taken salicylates within twenty-four hours of a massive hæmorrhage. In contrast, Waterson (1955) incriminated aspirin as a causal factor in only 3 of a series of 170 cases of major gastrointestinal hæmorrhage.

As some 4000 million salicylate tablets are said to be consumed annually in Great Britain, the possible relation of this drug to gastrointestinal hæmorrhage is important. Earlier work is inconclusive.

Evidence has been of necessity statistical, and control has often been inadequate because of the problem of assessing habitual salicylate consumption in a group reasonably comparable to patients with hæmatemesis and melæna. The reason for aspirin consumption is of particular relevance, as the drug may have been taken as a result of hæmorrhage for symptoms of blood loss, and accurate timing of the onset of bleeding is therefore important. Precise information regarding the site of bleeding, and its demonstration as a characteristic lesion due to salicylates, constitute the final criteria in the postulated relationship between these drugs and gastrointestinal hæmorrhage.

This paper reports a planned investigation of the relationship between salicylate consumption and gastrointestinal hæmorrhage in consecutive admissions to a community hospital, with careful attention to salicylate habits, both of the subjects studied and of a control group, and with extensive investigation directed particularly towards the causal lesions. In addition, the effects of salicylate compounds, soluble and insoluble, and non-salicylate analgesics on dyspeptic symptoms and stool occult-blood content have been studied in patients with peptic ulcer or with X-ray-negative dyspepsia and in controls. The appearance of the gastric mucosa at partial gastrectomy after salicylate ingestion has been compared with that in control specimens.

Material and Methods

Massive Gastrointestinal Hæmorrhage

121 patients were admitted to the department of gastroenterology of the Central Middlesex Hospital during the period January–July, 1957, with hæmatemesis and/or melæna. 18 patients were excluded from the study because of bleeding associated with trauma (2 patients), neoplasm of the upper gastrointestinal tract (5 patients), or œsophageal varices (2 patients), or because no reliable history was available (4 patients moribund and 5 patients with cerebral hypoxia). 103 patients thus remained in whom bleeding was thought to

TABLE I—AGE AND SEX OF PATIENTS WITH GASTROINTESTINAL HÆMORRHAGE AND OF OUTPATIENT CONTROLS

—	Gastrointestinal hæmorrhage group*	Controls†
Age (yrs.):		
<21	7	2
21–30	8	20
31–40	11	15
41–50	19	28
51–60	27	21
61–70	20	12
>70	18	5
	Total 103	Total 103
Sex:		
Male	67	67
Female	36	36

*Average age 55. †Average age 45.

be associated with acute or chronic peptic ulceration (tables I and II).

The onset of hæmorrhage was timed from symptoms of faintness or collapse, or, in their absence, from objective evidence of bleeding. Details of habitual salicylate consumption and salicylate consumption in the seventy-two hours before bleeding were taken immediately. These included the time the drug was taken, the number and type of tablets, the method of and reason for their consumption, and dyspeptic symptoms of intolerance, if any.

Salicylate habits and consumption within the preceding seventy-two hours in a control group complaining of dyspepsia, but not of gastrointestinal bleeding, were assessed in 103 consecutive new outpatients attending the gastroenterological clinic. This control group was identical in sex-distribution, and similar in regard to diagnosis, but of a younger age in relation to patients with hæmorrhage (tables I and II).

Barium swallow and meal examinations were carried out in all patients in both groups, except 18 who had operations or died as a result of hæmorrhage. In those with hæmorrhage, gastroscopy (40 patients), laparotomy (20 patients), and postmortem examination (2 patients) were performed where necessary for treatment or confirmation of the diagnosis. Acute ulceration was defined as a lesion not identifiable on barium meal, but seen at gastroscopy and visible, but not palpable, at laparotomy or necropsy.

Occult Gastrointestinal Bleeding

The effect of doses of salicylate and non-salicylate analgesics on dyspeptic symptoms and stool occult-blood content was investigated in 35 subjects; 14 had peptic ulcers; 6 had X-ray-negative dyspepsia; and 15, including 3 with pernicious anæmia, had no evidence of gastrointestinal disease. All were hospital patients or members of the staff, and analgesic compounds were given for the treatment of musculoskeletal and other disorders, or as an aid to diagnosis in some instances. Interrogation for dyspeptic symptoms and stool occult-blood determinations were carried out daily during five to seven day periods of treatment with aspirin *B.P.* (gr. 10 [0·7 g.] q.i.d.), soluble aspirin *B.P.* (gr. 10 [0·7 g.] q.i.d.), phenacetin *B.P.* (gr. 10 [0·7 g.] q.i.d.), and/or 'Panadol' (*N*-acetyl-*p*-aminophenol [Bayer] 1 g. q.i.d.), and during a control period of the same duration without medication. 29 patients received aspirin, and 12 were given soluble aspirin, and 15 of this group had a non-salicylate analgesic (phenacetin or panadol). 10 additional patients (3 controls, 3 with acute gastric ulcers, 2 with X-ray-negative dyspepsia, and 2 with chronic peptic ulcers (1 gastric and 1 duodenal)) received a course of 'Antidol' (salicylamide-[2-ethoxyethyl]-ether [Lewis Laboratories]) 1 g. t.d.s. under the same circumstances, but without additional salicylate therapy. A diet which excluded red meat and spinach was prescribed and two days elapsed before fæces were collected.

TABLE II—DIAGNOSIS IN PATIENTS WITH GASTROINTESTINAL HÆMORRHAGE AND OUTPATIENT CONTROLS

Lesion	Gastrointestinal hæmorrhage group			Controls
	"Salicylate-positive"	"Salicylate-negative"	Total	
None found	17 (35%)	6 (11%)	23	38
Acute gastric ulcer	7 (14%)	10 (19%)	17	—
Chronic gastric ulcer	4 (8%)	8 (15%)	12	9
Duodenal ulcer	18 (37%)	23 (43%)	41	44
Duodenal ulcer and acute gastric ulcer	—	1	1	—
Duodenal ulcer and chronic gastric ulcer	—	2	2	—
Stomal ulcer	1	2	3	3
Hiatus hernia	1	2	3	2
Hiatus hernia and chronic gastric ulcer	1	—	1	—
Gallstones	—	—	—	7
Total	49	54	103	103

The local action of salicylates on the stomach was studied at partial gastrectomy for peptic ulcer. 4 patients received aspirin *B.P.* (gr. 10 q.i.d.) for five days before the operation and with the premedication. 8 patients, for control purposes, received no salicylate. In both groups the stomach was scrutinised immediately for mucosal damage and, when indicated, histological appearances were examined.

Stools were tested "blind" by the method of Gregersen (1919) using benzidine, barium peroxide, and glacial acetic acid. The appearance of a blue colour within five seconds was regarded as a ++ response and within fifteen seconds as +. After this the result was regarded as negative. By these strict criteria it was hoped to exclude the false positives, due to the extreme sensitivity of the test, inherent in the sixty-second interval originally recommended. The analgesic compounds studied gave no reaction on in-vitro testing with the reagent.

TABLE III—RECENT SALICYLATE CONSUMPTION IN PATIENTS WITH GASTROINTESTINAL HÆMORRHAGE AND OUTPATIENT CONTROLS

Time (hr.) before hæmorrhage	Gastrointestinal hæmorrhage group	Controls
<12	35 } 49*	1 } 7
12–24	14 }	6 }
24–48	4	4
48–72	2	6
	55	17
None consumed	48	86
Total	103	103

*"Salicylate-positive" group.

Results

Major Gastrointestinal Hæmorrhage and Salicylates

55 of the hæmorrhage group had taken salicylates during the seventy-two hours prior to hæmorrhage, whereas 17 of the control group had consumed the drug within seventy-two hours of attending hospital. There was no striking difference in salicylate consumption during the period of twenty-four to seventy-two hours before the onset of bleeding. In contrast, the twenty-four hours immediately before hæmorrhage appeared particularly important. 49 of 103 patients had taken a salicylate preparation during this time, whereas only 7 of the outpatient control group had consumed salicylates within twenty-four hours of attending hospital. The majority of those bleeding had taken tablets within twelve hours of hæmorrhage (table III).

There was some difference in diagnosis in relation to salicylate consumption within twenty-four hours of hæmorrhage (table II). In particular, "acute lesions", either a proven acute gastric ulcer or no demonstrable gastroduodenal lesion, were more prominent (49%) in the "salicylate-positive" group (patients who had taken salicylates within twenty-four hours of hæmorrhage) than in the group bleeding without a history of recent salicylate consumption (30%). The site of bleeding was positively identified in 20 patients who came to laparotomy; of 8

patients who had bled in relation to salicylate consumption 7 had acute gastric ulcers, whereas of 12 patients whose hæmorrhage was unrelated to the drug only 4 had acute lesions. Evidence from gastroscopy was equivocal. Of 18 patients bleeding after salicylates 10 were in the " acute lesion " group, but an acute ulcer was displayed only once. In the " salicylate-negative " group (patients who had taken no salicylate within twenty-four hours of hæmorrhage) 12 of 22 patients were assumed to have acute lesions, and acute ulcers were seen on 6 occasions. No previous dyspeptic history was obtainable in 17 of 49 patients in the " salicylate-positive " hæmorrhage group, compared with only 9 of 54 in the " salicylate-negative " group.

The severity of bleeding was unrelated to salicylate consumption, and more than 80% of patients in both " salicylate-positive " and " salicylate-negative " hæmorrhage groups required blood-transfusion, an average of 5 pints being given to each patient in both groups. Review of the blood-groups showed no striking difference. Additional factors of possible significance included the type of salicylate preparation taken, the method of taking it, and the relationship of hæmorrhage after salicylate to symptoms of intolerance of the drug (table IV). The proportion of patients who took salicylates by swallowing

TABLE IV—ADDITIONAL FACTORS IN RELATION TO SALICYLATE CONSUMPTION

Factor	" Critical " tablets salicylate-positive group (49 patients) (%)	Usual tablets in controls (74 patients) (%)
Type of tablet:		
Soluble aspirin	8	3
Insoluble aspirin	92	97
Administration:		
Crushed or dissolved	12	22
Whole with drink	66	58
Whole without drink	22	20
Dyspepsia after:		
Present	4	23
Absent	96	77

tablets whole (without water) in both the " salicylate-positive " group and the outpatient controls was similar. Dyspeptic symptoms of intolerance (epigastric pain, acid regurgitation, nausea, or flatulence) to the salicylate taken before bleeding were remembered by only 2 of 49 patients in the " salicylate-positive " group, but 17 of 103 outpatients had experienced such symptoms at some stage.

A remarkable variety of salicylate preparations were taken. Soluble preparations had been taken by 4 patients who bled shortly afterwards, and were preferred habitually by 2 of the outpatient controls. Habitual salicylate consumption in the combined hæmorrhage groups was similar to that in the outpatient group (table V). However, the " salicylate-positive " hæmorrhage group contained more heavy consumers of salicylates than the " salicylate-negative " hæmorrhage group, although the majority of patients bleeding after salicylates took the drug rarely (table V). The majority of the " salicylate-positive " group had taken the " critical " tablets for their habitual reasons, and there was no evidence that the drug had been taken because of symptoms of bleeding (table VI). Although varied, the purposes for which salicylates were consumed habitually were comparable in the " salicylate-positive " and outpatient groups.

Specimens resected at partial gastrectomy for peptic ulcer from patients who had received salicylate preoperatively, and from those who had not, showed that acute mucosal ulceration or hæmorrhage, or both, were

TABLE V—HABITUAL SALICYLATE CONSUMPTION

Tablets per year	Gastrointestinal hæmorrhage			Controls
	" Salicylate-positive "	" Salicylate-negative "	Total	
<50	28 (57%)	28 (52%)	56	56
51–100	5 (10%)	—	5	6
101–300	10 (21%)	—	10	4
>300	6 (12%)	2 (4%)	8	8
None	—	24 (44%)	24	29
Total	49	54	103	103

comparable in both groups. In 8 control specimens (5 patients with duodenal ulcer, 2 patients with gastric ulcer, and 1 patient with combined gastric and duodenal ulcers) acute lesions of the gastric mucosa were found on 3 occasions. 1 patient with a gastric ulcer and 1 with a duodenal ulcer showed acute ulcers, and the other patient with a gastric ulcer showed areas of mucosal hæmorrhage without visible ulceration. 4 patients (2 with gastric, and 2 with duodenal ulcers) received aspirin preoperatively, and acute ulceration was found in 1 specimen which also contained a chronic gastric ulcer. The relatively high incidence of changes in the control group, attributable to pathological processes, intubation of the stomach, or surgical trauma, discouraged the extension of this study.

Hæmatological investigations were carried out in 8 patients in whom massive gastrointestinal hæmorrhage or ++ positive stool occult-blood results had occurred in relation to salicylate consumption. No change in prothrombin content, bleeding-time, or clotting-time was observed during the two hours after the ingestion of soluble aspirin *B.P.* (gr. 10) in any patient.

Occult Gastrointestinal Bleeding and Salicylates

The results of stool occult-blood estimations following the administration of different analgesics to various groups of patients are shown in table VII. During control periods, a ++ response was not seen, but consumption of aspirin *B.P.* or soluble aspirin *B.P.* was followed by the appearance of ++ occult blood in the stools in 18 of 35 subjects. In contrast, phenacetin *B.P.* or panadol produced ++ occult bleeding on only one occasion. Aspirin *B.P* provoked a ++ response in 13 of 29 patients (19% of stools tested) and soluble aspirin *B.P.* in 6 of 12 patients (20% of stools tested). During treatment with phenacetin, 1 of 7 patients had a ++ response, on one occasion only (3% of stools tested), but none of 13 patients taking panadol showed a ++ result. In the control periods, 18% of stools tested gave a + response, in comparison with 20% with aspirin, 22% with soluble aspirin, 11% with phenacetin, and 9% with panadol.

No difference in the stool occult-blood response to salicylates was found between patients with earlier major gastrointestinal hæmorrhage related or unrelated to

TABLE VI—REASONS FOR SALICYLATE CONSUMPTION

—	Salicylate-positive hæmorrhage group		Controls
	Recent salicylate	" Usual " salicylate	
Headache	18 (37%)	22 (45%)	47 (64%)
Musculoskeletal pain	12 (24%)	10 (20%)	9 (12%)
Insomnia	2	2	5
Coryza	6	6	6
Dyspepsia, toothache, phlebitis, bereavement	4	2	1
Malaise, lassitude, dizziness, shivering	7 (14%)	7 (14%)	6
Total	49	49	74

salicylates, with peptic ulcer, or with X-ray-negative dyspepsia, or controls without gastrointestinal symptoms. 15 patients received both aspirin and non-salicylate analgesics; 7 of these (3 with gastrointestinal symptoms and 4 controls) had ++ responses (17% of stools tested) during treatment with aspirin (7 patients) or soluble aspirin (1 patient), while only one ++ result occurred in 107 stools tested during treatment with phenacetin or panadol in these subjects. In 9 additional patients (not shown in table VII) who received antidol, stool occult-blood results were comparable in control periods and during treatment and no ++ response occurred. Of 3 patients with pernicious anæmia and achlorhydria, 1 had occult blood in the stool during the administration of aspirin. Minor dyspeptic symptoms of intolerance occurred in 3 of 55 patients (table VII), and this was unrelated to the appearance of occult blood in the stools or to the analgesic used.

Discussion

Incrimination of salicylates in the pathogenesis of massive gastrointestinal bleeding is supported by this study, and consumption of the drug could have accounted for hæmatemesis and/or melæna in over 40% of the patients studied. Definition of a causal relationship between salicylates and massive gastrointestinal hæmorrhage necessitates excluding the possibility that the drug was taken incidentally. The outpatient control group, although younger, proved to be surprisingly comparable with the hæmorrhage group, and age appears irrelevant in this instance as aspirin consumption is greatest in the second and third decades (A. Cartwright, personal communication). Statistical comparison of salicylate habits between the outpatients and those bleeding showed a very high incidence of salicylate consumption in the twenty-four hours before hæmorrhage. This is compatible with a causal relationship and could not be explained convincingly on other grounds. In addition, the frequency of occult gastrointestinal bleeding during salicylate consumption supports a direct association. Symptomatic inquiry excluded as far as possible the likelihood that salicylates were taken as a result of bleeding, but early symptoms of hæmorrhage are often non-specific and this remains an important consideration. Very frequent consumers of salicylates were more often found in the " salicylate-positive " hæmorrhage group, and, whilst this might conceivably reflect their habitual use of the drug alone, such patients equally must run a greater hazard of hæmorrhage.

The liability to hæmorrhage within twenty-four hours of taking salicylate suggests an acute lesion, and this accords with the greater number of patients with negative radiological findings in the " salicylate-positive " hæmorrhage group and with the occult bleeding soon after salicylate medication. However, it was not possible to demonstrate a characteristic lesion due to salicylates despite thorough investigation.

80% of the patients with major hæmorrhage after salicylate consumption had proven duodenal or chronic gastric ulcers, or dyspeptic histories. This susceptibility of patients with ulcers agrees with the experience of Muir and Cossar (1955). They recommended for such patients soluble calcium aspirin, which appeared to be less irritant than standard aspirin and provoked fewer dyspeptic symptoms of intolerance. Such symptoms were relatively rare in all groups in the present series and seldom correlated with either occult bleeding during daily salicylate consumption or the onset of massive gastrointestinal hæmorrhage. Moreover there was no evidence that

TABLE VII—STOOL OCCULT-BLOOD FINDINGS DURING THERAPY WITH SALICYLATES AND NON-SALICYLATE COMPOUNDS

Clinical manifestations	Case no.	Diagnosis	Control period			Aspirin *B.P.*			Soluble aspirin *B.P.*			Phenacetin *B.P.*			Panadol		
			++	+	−ve	++	+	−ve	++	+	−ve	++	+	−ve	++	+	−ve
Hæmatemesis and/or melæna within 24 hr. of salicylate consumption	1	Duodenal ulcer			3			6						6			
	2	" "			4	2	1	3			4						
	3	" "		2	3			5				1	1	3			
	4	" "			3	1	4										
	5	X-ray-negative dyspepsia			5		1	2									
	6	Acute erosive gastritis			4			3									
Hæmatemesis and/or melæna unrelated to salicylates	7	Duodenal ulcer		2	3				4		1						
	8	X-ray-negative dyspepsia			5	3		1					3	1		2	3
	9	" " "		2	3				3		1*						
	10	" " "			4						3						
Chronic dyspepsia without major bleeding	11	Duodenal ulcer			6		1	6		1	4			5		1	5
	12	" "		8		1	3			7							
	13	" "		3	3	1	1	3	2	2	1			6		2	3
	14	" "			7			7		1	6			7			7*
	15	" "			3				1	1	1						
	16	" "			7			7			5*			5			6
	17	Gastric ulcer			4				1		4						
	18	Stomal ulcer		1	4		4	1									
	19	X-ray-negative dyspepsia		3	3	5	1	2									
	20	" " "		5	2	1	2	3									5
	21	Control without dyspepsia			6				1	1	3						
	22	" " "			5			5									
	23	" " "			3		1	3									
	24	" " "				1	3	3									7
	25	" " "						4									3
	26	" " "				3	1	2									6
	27	" " "					1	6								1	6
	28	" " "				2	3	1									4
	29	" " "				6	1	1									4
	30	" " "					1	1									4
	31	" " "			6			6									
	32	" " "			6	3	2	2									
	33	Pernicious anæmia			6			6									
	34	" "			6	2		4									
	35	" "			6		1	5									
Total			—	26	120	31	32	98	12	13	33	1	4	33	—	6	63

*Dyspeptic symptoms attributed to therapy.
++, +, −ve = result of test for occult blood. Numerals below refer to number of specimens tested.

soluble aspirin was less likely to provoke a major hæmorrhage, and both soluble aspirin and standard aspirin were equally liable to produce ++ occult bleeding during treatment. This was found not only in 7 of 14 peptic-ulcer patients, but also in a similar proportion of 21 dyspeptics or controls. The observation that salicylate compounds may cause occult bleeding was made simultaneously by Lange (1957), who studied subjects without gastrointestinal disease, and he confirmed that no added protection was afforded by soluble or other aspirin preparations.

In contrast, occult bleeding was found in only 1 of 7 patients when phenacetin was given, and never occurred in 22 patients receiving panadol or antidol, thus emphasising the importance of prescribing suitable non-salicylate analgesics when possible, particularly for dyspeptic subjects. The presence or absence of symptoms of intolerance was in our experience no reliable indication of the liability to major or occult gastrointestinal bleeding during salicylate therapy.

Douthwaite and Lintott (1938) and Hurst and Lintott (1939) found hæmorrhagic gastritis on gastroscopy following aspirin administration, but this was not confirmed by Paul (1943). Muir and Cossar (1955) considered that salicylates produced an acute erosive gastritis, not only from the appearance of gastrectomy specimens after the preoperative administration of specially insoluble aspirin tablets, but also because blood loss in their patients was usually trivial. In this series the rather higher proportion of the " acute lesion " group in those bleeding after salicylates supports the concept of an acute process. However, hæmorrhage was usually severe and the great majority of patients required blood-transfusion, implying that either acute ulcers, which may bleed profusely (Avery Jones and King 1953) or exacerbations of chronic ulcers were responsible.

Gastroscopy was of little assistance in defining the bleeding site, but it is probably important that 7 of 8 patients requiring surgical treatment because of the severity of hæmorrhage after salicylate consumption had acute gastric ulcers. The examination of routine gastrectomy specimens after the administration of aspirin *B.P.* was less conclusive, owing to the frequent presence of hæmorrhages and acute erosions in control specimens.

Transient occult bleeding, presumably from minor lesions in the upper gastrointestinal tract, readily followed salicylate consumption in all groups of patients, but the majority of those bleeding massively after salicylates had chronic peptic ulcers or a previous history of dyspepsia. This suggests that factors responsible for chronic ulcer production, such as impaired mucosal resistance or increased acid-pepsin secretion, may enhance the development of acute ulceration from a salicylate-induced gastritis in some patients, and thus determine the heavier bleeding. In addition to acute lesions of the stomach or, possibly, the duodenum and elsewhere, salicylates may cause bleeding from pre-existing chronic ulcers, either by a local action or by stimulating gastric secretion.

Although gastritis or ulceration is usually attributed to an irritant action by salicylate particles on the gastric mucosa, systemic effects of salicylates might contribute or could even constitute a major factor. Warthin (1954) postulated an allergic reaction, and this could account for gastric ulceration in rats induced by subcutaneous salicylate injections (Barbour and Dickerson 1938). Ivy et al. (1950) and Muir and Cossar (1955) demonstrated increased gastric acidity in response to oral salicylates, an action which might exacerbate a chronic peptic ulcer or contribute to the formation of an acute lesion; but the occult bleeding which followed aspirin in one of our patients with pernicious anæmia cannot be explained on this basis. Hypoprothrombinæmia follows large doses of salicylates in man (Shapiro et al. 1943), and a therapeutic dose has been reported to cause bleeding by this mechanism (Smith and McKinnon 1951). No alteration in prothrombin times was demonstrated in this study when major hæmorrhage or occult bleeding occurred in response to salicylates.

Salicylates also have central effects which include an antipyretic action, thought to be mediated through the hypothalamus, and nausea (Caravati and Cosgrove 1946). Gastric ulceration was produced by A. D. Keller (cited by Cushing 1952) in cats following brain section below the hypothalamic centres, and a central action by salicylate might therefore be relevant to acute gastric ulceration in man.

Certain actions of salicylate closely resemble those of adrenal corticoid drugs, and dyspepsia and peptic-ulcer breakdown is considered a hazard of steroid therapy. Cortisone-like actions of salicylate have been demonstrated (Roskam et al. 1951, Van Cauwenberge 1951), and such effects may contribute to hæmorrhage in patients with peptic ulcers. Nevertheless, it is possible that peptic ulcer and its complications in some patients, particularly those with chronic rheumatoid conditions, may sometimes be related to concurrent salicylate medication rather than to steroid therapy. In this respect, the occult bleeding in response to aspirin medication also raised the possibility that anæmia in acute and chronic rheumatoid conditions may occasionally be related to treatment rather than to the disease itself, and occult-blood loss in the stools from long-term salicylate consumption appeared to be the cause of chronic anæmia in 2 patients reported by Summerskill and Alvarez (1958).

Summary

A controlled investigation supported a causal relationship between salicylate consumption and massive gastrointestinal hæmorrhage from peptic ulcer. Salicylates could be incriminated in over 40% of 103 consecutive patients admitted to hospital with hæmatemesis and/or melæna associated with peptic ulcer.

The lesion induced by salicylate was difficult to define at gastroscopy or at partial gastrectomy. The clinical history, together with findings at emergency partial gastrectomy, indicated that acute erosions in the stomach, and possibly lower in the gastrointestinal tract, were sometimes responsible, although activation of a pre-existing chronic peptic ulcer often seemed likely. No alteration in prothrombin-time due to salicylates was found in patients with gastrointestinal bleeding.

Occult-blood loss in the stools occurred during periods of salicylate consumption in approximately 50% of patients with peptic ulcer or X-ray-negative dyspepsia and of controls. Patients with previous dyspepsia were more liable to massive hæmorrhage, but occult bleeding occurred equally in all groups. Both soluble and insoluble aspirin caused occult bleeding, but non-salicylate analgesics (' Phenacetin ', ' Panadol ', and ' Antidol ') did not influence the stool occult-blood content. There was no evidence that soluble aspirin reduced the risk of major bleeding; neither were dyspeptic symptoms of intolerance

nor the method of taking salicylate preparations related to the occurrence of hæmatemesis and melæna.

We are very grateful to Dr. F. Avery Jones and Dr. W. R. S. Doll for encouraging this investigation and for their advice. The consultant staff of the Central Middlesex Hospital kindly permitted us to study the patients and cooperated generously with the surgical, radiological, and hæmatological findings. 'Antidol' tablets were supplied by Lewis Laboratories Ltd., and Bayer Products Ltd. made available the 'Panadol' tablets.

REFERENCES

Barbour, H. G., Dickerson, V. C. (1938) *Arch. Int. Pharmacodyn.* **58**, 78.
Brown, R. K., Mitchell, N. (1956) *Gastroenterology*, **31**, 198.
Caravati, C. M., Cosgrove, E. F. (1946) *Ann. intern. Med.* **24**, 638.
Cushing, H. (1932) *Surg. Gynec. Obstet.* **55**, 1.
Douthwaite, A. H. (1938) *Brit. med. J.* i, 1143.
— Lintott, G. A. M. (1938) *Lancet*, ii, 1222.
Gregersen, J. P. (1919) *Arch. VerdauKr.* **25**, 169.
Hurst, A. (1943) *Lancet*, ii, 768.
— Lintott, G. A. M. (1939) *Guy's Hosp. Rep.* **89**, 173.
Ivy, A. C., Grossman, M. I., Bachrach, W. H. (1950) Peptic Ulcer. London.
Jones, F. Avery (1952) Modern Trends in Gastroenterology. London.
— King, W. E. (1953) *Aust. Ann. Med.* **2**, 179.
Kelly, J. J., Jr. (1956) *Amer. J. med. Sci.* **232**, 119.
Lange, H. F. (1957) *Gastroenterology*, **33**, 770.
Muir, A., Cossar, I. A. (1955) *Brit. med. J.* ii, 7.
Raul, W. D. (1943) *J. Iowa St. med. Soc.* **33**, 155.
Richmond, H. A. J. (1950) *Brit. med. J.* i, 439.
Roskam, J., Van Cauwenberge, H., Musters, A. (1951) *Lancet*, ii, 375.
Shapiro, S., Redish, M. H., Campbell, H. A. (1943) *Proc. Soc. exp. Biol., N.Y.* **53**, 251.
Smith, J. M., MacKinnon, J. (1951) *Lancet*, ii, 569.
Summerskill, W. H. J., Alvarez, A. S. (1958) *Lancet*, ii, 925.
Van Cauwenberge (1951) *ibid.* ii, 374.
Warthin, T. A. (1954) Cited by Kelly, J. J.
Waterson, A. P. (1955) *Brit. med. J.* ii, 1531.

"SALICYLATE ANÆMIA"

W. H. J. SUMMERSKILL
M.A., D.M. Oxon., M.R.C.P.
SENIOR REGISTRAR

A. S. ALVAREZ
M.B. Birm.
HOUSE-PHYSICIAN

DEPARTMENT OF GASTROENTEROLOGY,
CENTRAL MIDDLESEX HOSPITAL, LONDON, N.W.10

CONSUMPTION of salicylate compounds causes occult gastrointestinal bleeding (Lange 1957, Alvarez and Summerskill 1958) in a considerable proportion of patients, and, much less frequently, hæmatemesis or melæna occurs as a result of medication (Muir and Cossar 1955, Alvarez and Summerskill 1958). We describe here 2 patients with severe "iron-deficiency" anæmia due to gastrointestinal hæmorrhage associated with the taking of salicylates.

Methods

The hæmatological, biochemical, and radiological investigations reported are standard procedures. The regime during collection of fæces, and the modified interpretation of the stool occult-blood content by the method of Gregersen (1919), are described elsewhere (Alvarez and Summerskill 1958).

Case-reports

Case 1 (fig. 1).—A man, then aged 39, was admitted to hospital in July, 1953, complaining of recent fatigue and exertional dyspnœa. For seven years he had suffered from migrainous headaches for which he took an average of 8–10 salicylate tablets weekly, and he had also had recurrent attacks of diarrhœa (without blood or mucus in the stools) since leaving the Army in 1945. His previous history was otherwise unremarkable, and there was no abnormality on physical examination apart from anæmia. The hæmoglobin level was 56% (8·4 g. per 100 ml.) and there were hæmatological features of iron deficiency. Full investigation, including a careful dietary history, failed to reveal the cause of the anæmia, and, after responding to intravenous iron therapy, he was discharged to the outpatient department where this treatment was followed by oral iron.

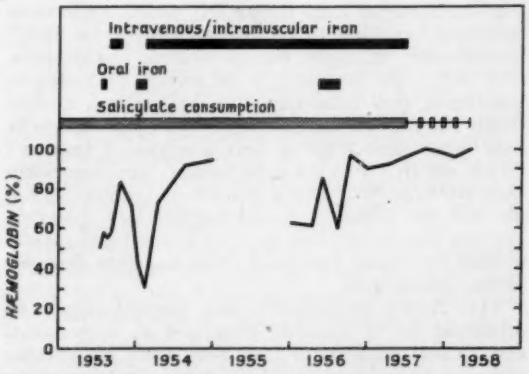


Fig. 1—Hæmoglobin levels, salicylate consumption, and iron therapy in case 1.

Despite this, he was readmitted to hospital within six months with severe anæmia (hæmoglobin 29% [4·2 g. per 100 ml.]) associated with congestive heart-failure. Laparotomy was seriously considered, as full investigation failed to show the cause of the anæmia, but he again responded well to intravenous iron. On leaving hospital, he continued to receive iron injections regularly until January, 1956, when he again complained of fatigue, and was readmitted to hospital with a hæmoglobin level of 63% (9·3 g. per 100 ml.). As before, treatment with intravenous iron was successful, and he left hospital after further investigation to continue iron injections as an outpatient.

The investigations carried out were as follows: serial stool-occult bloods (on each of three hospital admissions), negative; barium meal and follow-through (on three occasions), negative; barium enema, negative; fractional test-meal contained free acid (twice); sigmoidoscopy, glucose-tolerance curve, jejunal biopsy, examinations of stools for acid-fast bacilli, chest X-rays, numerous examinations of the urine (including tests for urobilinogen), and repeated estimations of serum-bilirubin, serum-protein, serum-electrolyte, blood-urea, and erythrocyte-sedimentation rate all showed no abnormality.

Comment

The appearance of the sternal marrow and the findings in the peripheral blood (see accompanying table) in May, 1954, were reported by Dr. G. Discombe and Dr. D. L. Mollin as compatible with iron-deficiency anæmia (treated with iron), hæmolytic anæmia due to chronic hæmorrhage.

The lack of objective evidence of blood-loss, the negative stool occult-blood tests, and the failure to demonstrate a culpable lesion were thought to exclude anæmia due to hæmorrhage. Similarly, the normal red-cell survival-time and fragility, together with the absence of bilirubinæmia or increased urinary urobilinogen, eliminated the likelihood of hæmolytic anæmia.

Although "primary" iron-deficiency anæmia was therefore diagnosed, there are several atypical features. Such anæmia rarely, if ever, arises de novo in a man of 39 taking an adequate diet (Wintrobe 1951, Discombe 1955). Moreover, the sudden fall in hæmoglobin level from 71% (10·5 g. per 100 ml.) to 29% (4·3 g. per 100 ml.) in just over seven weeks (Dec. 15, 1953–Feb. 6, 1954) could not be due to iron deficiency alone, as the patient had received intravenous iron ('Ferrivenin' 0·9 g.) two months previously and was taking oral iron ('Colliron' 1 drachm t.d.s.) at the time. If only 10 mg. or less of

iron was absorbed daily during this period, there must have been blood-loss of approximately 50–90 ml. daily. Furthermore, he again became anæmic (hæmoglobin 63% [9·3 g. per 100 ml.]) in December, 1955, despite intravenous iron (ferrivenin 100 mg.) at two to four weekly intervals throughout the previous year. Immediately after responding to iron injections ('Imferon' 1·25 g. and ferrivenin 0·9 g.) in hospital, the hæmoglobin again fell from 85% (12·6 g. per 100 ml.) to 60% (8·9 g. per 100 ml.) within three months, although continued oral iron (ferrous sulphate gr. 6 t.d.s.) was being supplemented by regular intravenous iron injections from his general practitioner.

This failure of adequate iron therapy cannot be accounted for by impaired absorption or utilisation of iron. Large amounts of iron were given by systemic routes; between July 7 and 23, 1953, the hæmoglobin rose from 46% (6·8 g. per 100 ml.) to 58% (8·6 g. per 100 ml.) on oral iron therapy alone, and later there was always a prompt response to systemic iron therapy in hospital. In addition, repeated fat balances yielded no evidence of intestinal malabsorption, and free hydrochloric acid was twice demonstrated in the gastric secretion. Although accurate records of all the doses of iron administered at various times are not available, an additional or alternative cause for the anæmia seemed likely and the relationship between the patient's heavy consumption of salicylate compounds and the anæmia was investigated.

HÆMATOLOGICAL FINDINGS IN CASES 1 AND 2

—	Case 1	Case 2
Hæmoglobin (g. per 100 ml.)	7·9 (53%)	5·6 (38%)
Red cells (million per c.mm.)	2·7	..
Hæmatocrit (%)	27	24
Mean corpuscular volume	100	..
Mean corpuscular hæmoglobin concentration (%)	29	23
Reticulocytes (%)	2	1
Erythrocyte cytology	Anisocytosis, microcytosis, hypochromia	Anisocytosis, microcytosis, poikilocytosis, hypochromia
Red-cell fragility	Normal curve	Normal curve
White cells (per c.mm.)	3000	3500
Platelets (per c.mm.)	178,000	200,000
Sternal marrow	Erythropoietic hyperplasia with macronormoblastic reaction	..
COAGULATION STUDIES		
Before calcium aspirin:		
Prothrombin content (%)	>50	> 50
Bleeding-time (Duke's method) (min.)	2½	3
Clotting-time (capillary method) (min.)	7	3½
After calcium aspirin gr. 10 by mouth:		
Prothrombin content (%)	> 50	> 50
Bleeding-time (min.)	2¾	4
Clotting-time	7¾	5
Red-cell survival time	Normal	..
Radioactive-iron-absorption test	..	Low normal

The administration of one of the salicylate compounds habitually used by the patient for headaches in its customary dosage (aspirin *B.P.* gr. 10 t.d.s.) converted the stool occult-blood reaction from negative to strongly positive on two occasions (fig. 2). This occurred after one and after three days' treatment, and on the second occasion the occult-blood reaction reverted to normal as soon as the drug was stopped. There was no alteration in the prothrombin content, bleeding-time, or clotting-time following salicylate administration (see accompanying table). More specific confirmation of the relationship between salicylate consumption and the anæmia resulted from the cessation of iron therapy and (apart from occasional lapses) of salicylate medication. During the ten-month period that has followed, regular hæmoglobin estimations have shown no recurrence of anæmia (fig. 1), and there is no evidence of iron deficiency in the blood-film.

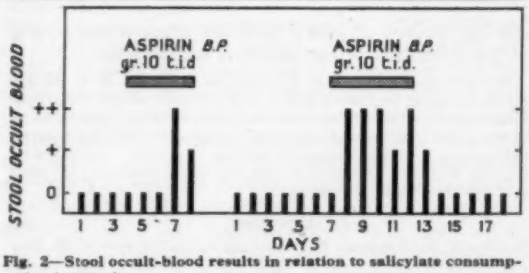


Fig. 2—Stool occult-blood results in relation to salicylate consumption in case 1.

Case 2 (fig. 3).—A housewife, then aged 29, was first admitted to hospital for the investigation and treatment of anæmia and dyspepsia in 1948. Apart from the recent onset of fatigue and exertional dyspnœa, she complained of recurrent epigastric pain and acid regurgitation during the previous months. These symptoms occurred within an hour of eating and were partially relieved by antacids. For a year she had had severe headaches, for which she took up to 30 salicylate tablets weekly, and the dyspepsia often coincided with the headaches. Since her last (fourth) pregnancy in 1945, she had had menorrhagia, and an earlier confinement had been complicated by hæmorrhage for which she received a blood-transfusion and iron tablets. Her childhood had been spent in difficult financial circumstances, but her nutritional history was adequate. Physical examination showed severe anæmia and epigastric tenderness. The hæmoglobin was 38% (5·6 g. per 100 ml.), apparently owing to iron deficiency, and there was an immediate reticulocyte response (11%) to oral iron therapy. No cause for the dyspepsia was found.

After leaving hospital she attended the outpatient department regularly. The anæmia recurred and required continuous oral iron therapy, on two occasions supplemented by intravenous iron. Because of the severity of the anæmia and its possible relationship to the menorrhagia, dilatation and curettage were performed in 1951, and, in the absence of improvement, a total hysterectomy was undertaken in the following year. She remained anæmic, however, and, as the dyspepsia persisted, laparotomy with a view to partial gastrectomy for a suspected peptic ulcer was considered, despite repeatedly negative X-ray and stool occult-blood findings. In

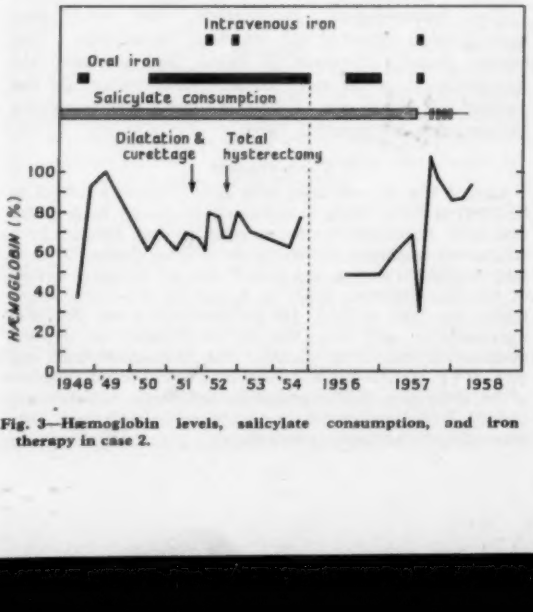


Fig. 3—Hæmoglobin levels, salicylate consumption, and iron therapy in case 2.

1956 she became severely anæmic (hæmoglobin 48% [7·4 g. per 100 ml.]) again and there was no response to a six-month course of oral iron, although the anæmia improved subsequently when iron therapy was stopped. A further episode of severe anæmia (hæmoglobin 29% [4·2 g. per 100 ml.]) in June, 1957, resulted in her admission to hospital for further investigation and assessment.

During the period of observation the following investigations were carried out: Barium meals (on six occasions), once with a "follow-through", and a barium enema showed no abnormality. Serial stool occult-blood tests were negative on four occasions, free hydrochloric acid in the stomach was demonstrated with a fractional test-meal, and gastric biopsy showed only mild atrophic changes in the gastric mucosa. No abnormality was found on gastroscopy or sigmoidoscopy, and a radio-opaque string passed into the duodenum did not become bloodstained. The fæcal-fat content and the absorption of radioactive iron were within normal limits.

Comment

As in case 1, the findings were those of an iron-deficiency anæmia (see table) for which no cause could be demonstrated. Following hysterectomy, which failed to improve the anæmia, there was no objective evidence of blood-loss, and very full investigation of the gastro-

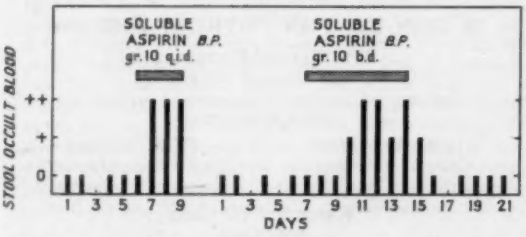


Fig. 4—Stool occult-blood results in relation to salicylate consumption in case 2.

intestinal tract, including repeatedly negative stool occult-blood examinations, showed no possible site of bleeding. Hæmolytic anæmia was excluded by the absence of bilirubinæmia or excess urobilinogen in the urine, a normal red-cell fragility curve, and a negative Coombs test. Her responses to oral iron, together with a normal radioactive-iron-absorption test and fæcal-fat content, showed that intestinal absorption was unimpaired.

"Primary" iron deficiency appeared unlikely as the diet was adequate, and, in addition, there were features suggesting intermittent blood-loss. There was a good response to oral iron therapy (ferrous sulphate gr. 6 t.d.s.) in hospital in July, 1948, although on two subsequent occasions it was necessary to prescribe intravenous iron (ferrivenin 0·6 g. and 0·8 g.) in addition to adequate oral iron treatment (ferrous sulphate gr. 6 t.d.s., ferrous gluconate 300 mg. t.d.s., or colliron 1 drachm t.d.s.) in the outpatient department. Furthermore, the same amount of oral iron had no effect in the latter months of 1956, although there was hæmatological improvement immediately afterwards, when iron therapy had been stopped. Finally, the abrupt fall in the hæmoglobin level from 62% (9·2 g. per 100 ml.) to 29% (4·2 g. per 100 ml.) in four weeks during May–June, 1957, can only be explained by blood-loss. It may be relevant that this coincided with unusually severe headaches, for which the patient took at least 30 tablets of soluble aspirin weekly, and an exacerbation of her dyspepsia.

The possible relationship between the anæmia and salicylate consumption was therefore investigated at this time. The administration of soluble aspirin *B.P.* (gr. 10 q.d.s.) was followed by strongly positive occult-blood reactions in the stools, the reaction having been negative during the preceding control period. When the observations were repeated with a smaller dose of soluble aspirin (gr. 10 b.d.), the stools again contained occult blood during salicylate medication, although none was present before or after treatment (fig. 4). While receiving salicylates, the patient complained of temporary recurrence of dyspeptic symptoms. A test dose of salicylate failed to alter blood-coagulation tests (see table).

After hospital treatment for the anæmia with ferrivenin (1·2 g.) in August, 1957, there was a satisfactory response, and no further iron therapy was given. At the same time the patient was advised not to take salicylate preparations and an alternative analgesic was suggested. During the subsequent four months the hæmoglobin level fell from 99% (14·6 g. per 100 ml.) to 76% (11·2 g. per 100 ml.). Although the level was still within the range for healthy women (16·8–11·0 g. per 100 ml.) described by Nelson (1937), the prescribed analgesic had often failed to relieve her headaches and she had been taking various preparations containing salicylates. Occult bleeding due to this could explain the fall in the hæmoglobin level. However, after renewed exhortations to avoid salicylates, which were more successful, but not altogether effective, the hæmoglobin level rose to 86% (12·7 g. per 100 ml.) after a further three months without iron therapy. Thus the hæmoglobin level has remained within normal limits without iron therapy for the seven-month period during which salicylate consumption was greatly reduced. The absolute indices at the end of this time showed no abnormality and there were only minor indications of iron deficiency in the blood-film.

Discussion

Chronic anæmia was presumed to be related to occult gastrointestinal bleeding due to salicylates in both patients. The diagnosis depended ultimately on the absence of hæmatological relapse when both iron therapy and salicylates had been withdrawn for seven months in one case and ten months in the other, but it was difficult to establish for several reasons. Routine stool occult-blood examinations were repeatedly negative while the patients were in hospital, as they were not taking their habitual salicylates. The appearance of occult blood in the stools during trial periods of salicylate therapy supported the diagnosis; but the test is relatively non-specific, as about 50% of healthy people or patients with peptic ulcer will produce positive stools under such circumstances (Alvarez and Summerskill 1958). Quantitative assessment of blood-loss in the fæces with isotopes is unlikely to help, as the degree of hæmorrhage after any one course of the drug cannot be assumed to be constant. Moreover, the multiplicity of salicylate compounds readily available to the public under different names, and the difficulty of finding equally effective non-salicylate analgesics, resulted in occasional self-medication with salicylates by both patients during the diagnostic period when complete withdrawal was attempted.

The trial of oral salicylate therapy was useful in case 2 as it related her dyspeptic symptoms to use of the drug. More often, however, such symptoms of intolerance are unrelated to either massive or occult gastrointestinal bleeding (Alvarez and Summerskill 1958). The use of soluble aspirin fails to eliminate the risk of massive or, as in this patient, occult gastrointestinal bleeding (Alvarez and Summerskill 1958); neither does it reduce the in-

cidence of dyspepsia or enhance the pharmacological action of salicylate (Batterman 1958).

Possible causes of bleeding after salicylates include erosive or hæmorrhagic gastritis (Douthwaite and Lintott 1938, Muir and Cossar 1955), but acute lesions could also occur lower in the gastrointestinal tract. Patients with chronic peptic ulcer or previous dyspepsia are particularly prone to massive hæmorrhage (Muir and Cossar 1955, Alvarez and Summerskill 1958), perhaps because more severe lesions result from increased acid-pepsin production by the stomach or impaired mucosal resistance, but occult bleeding apparently occurs equally in all groups of patients (Alvarez and Summerskill 1958). Hæmorrhage seemed to be irregular and relatively mild in the patients reported here; but it was extremely variable in a third patient, included in the earlier study, who exhibited both occult and massive bleeding. This 70-year-old woman had been receiving up to 14 salicylate tablets daily for seven years for the management of painful and crippling arthritis. In this time, eleven major episodes of hæmatemesis or melæna were superimposed on severe chronic iron-deficiency anæmia. During treatment with salicylates the stools usually contained occult blood and occasionally appeared tarry, whereas no abnormality was found during therapy with non-salicylate analgesics.

Neither patient reported here had noticed evidence of blood-loss, and at least 50 ml. blood must be present to impart a tarry appearance to the fæces (Daniel and Egan 1939), although greater hæmorrhage can occur slowly without the subjective recognition of melæna. The incidence of anæmia due to occult hæmorrhage from salicylates is unpredictable, but both salicylate consumption and iron-deficiency anæmia are common. Two factors are probably important, and both may have contributed to the development of anæmia in our patients. The risk is likely to be related to the amount of salicylate consumed, and it would therefore be greatest in patients with long-standing painful disabilities such as headache or musculoskeletal disorders. In addition, anæmia may develop more readily under these circumstances in patients with pre-existing impairment of iron absorption of utilisation.

These considerations stress the importance of eliciting a detailed history regarding prescribed therapy and self-medication, particularly in patients with anæmia attributed to primary iron deficiency, chronic blood-loss, or rheumatic diseases. If salicylate consumption is suspected as a causal factor, the effect of withdrawing the drug, where practicable, should be tried before treatment with iron or alternative procedures, such as total hysterectomy (which failed to influence the anæmia in case 2) or laparotomy (which was contemplated in both patients).

Summary

Severe " iron-deficiency " anæmia, of uncertain cause despite extensive investigation, had required continuous treatment with iron for 5 years and 10 years respectively in a man of 47 and a woman of 40. Laparotomy had been advocated in both patients, and total hysterectomy had failed to influence the anæmia in the woman.

Habitually heavy consumption of salicylate compounds for headaches had coincided with the onset and subsequent course of the anæmia in both patients.

Occult bleeding from the gastrointestinal tract was demonstrated during controlled periods of salicylate medication. After salicylate consumption had been greatly reduced, anæmia did not recur during follow-up periods of ten and seven months without iron therapy.

Salicylate consumption is therefore put forward as a possible cause of anæmia.

We are grateful to Dr. F. Avery Jones for permission to study these patients and for his encouragement. Dr. G. Discombe kindly gave us his advice regarding preparation of the data; Dr. L. Mollin and Dr. Mary Smith, of the Postgraduate Medical School of London, respectively reported on the sternal marrow in case 1 and carried out the iron-absorption test in case 2. The careful records kept by the patients' practitioners, Dr. Sheila Handel and Dr. A. S. Cook, were of great assistance to us.

Addendum

After further follow-up, the hæmoglobin levels remain within the normal range at 94% (13·9 g. per 100 ml.) in case 1 after 13 months, and at 86% (12·7 g.) in case 2 after 10 months.

REFERENCES

Alvarez, A. S., Summerskill, W. H. J. (1958) *Lancet*, ii, 920.
Batterman, R. C. (1958) *New Engl. J. Med.* **258**, 213.
Daniel, W. A., Egan, S. (1939) *J. Amer. med. Ass.* **113**, 2232.
Discombe, G. (1955) *Trans. med. Soc. Lond.* **71**, 63.
Douthwaite, A. H., Lintott, G. A. M. (1938) *Lancet*, ii, 1222.
Gregersen, J. P. (1919) *Arch. VerdauKr.* **25**, 169.
Lange, H. F. (1957) *Gastroenterology*, **33**, 770.
Muir, A., Cossar, I. A. (1955) *Brit. med. J.* ii, 7.
Nelson, C. F. (1937) *Amer. J. clin. Path.* **7**, 285.
Wintrobe, M. M. (1951) Clinical Hematology. Philadelphia.

A SKIN TEST IN THYROID DISEASE

W. WATSON BUCHANAN
M.B. Glasg., F.R.F.P.S.
HALL FELLOW, UNIVERSITY DEPARTMENT OF MEDICINE, GARDINER INSTITUTE

J. R. ANDERSON
B.Sc., M.D. St. And.
SENIOR LECTURER IN PATHOLOGY

R. B. GOUDIE
M.B. Glasg., M.R.C.P.
LECTURER IN PATHOLOGY

KATHLEEN G. GRAY
B.Sc. Glasg.
RESEARCH ASSISTANT, DEPARTMENT OF PATHOLOGY
UNIVERSITY OF GLASGOW

From the Western Infirmary, Glasgow

SOME patients with disease of the thyroid gland, and particularly those with Hashimoto's thyroiditis, have in their blood-serum circulating antibodies which react in vitro with components of human thyroid tissue. The phenomenon has been demonstrated by several observers using differing techniques: by the precipitin reaction (Roitt et al. 1956); by the complement-fixation reaction (Trotter et al. 1957, Goudie et al. 1957); and by Coon's fluorescent antibody technique (White 1957). Witebsky and his coworkers (Payne et al. 1957) have demonstrated similar antibodies by the agglutination of tanned red-blood-cells coated with antigen. We thought that an intradermal injection of an extract of human thyroid gland might give rise to a localised skin reaction in patients whose serum contained thyroid antibodies, and our results show that this is the case.

Material and Methods

Subjects

Skin tests were performed on 52 patients, of whom 33 (3 males and 30 females, aged twenty to sixty-eight years) had thyroid disease, and 19 (3 males and 16 females, aged forty-two to eighty-two years) served as controls. All the control patients had terminal illnesses without clinical evidence of thyroid disorder. The 33 patients with thyroid disease included 11 cases of Hashimoto's disease, 8 of primary myxœdema, 7 of thyrotoxicosis, 3 of simple non-toxic goitre, and 1 of thyroid carcinoma. The clinical and histological criteria for diagnosis were those used by Goudie et al. (1957). 3 patients did not readily fit into any of the diagnostic groups and were recorded as " unclassified " (table 1). The 1st of these was hypothyroid

TABLE I—RESULTS OF PRECIPITIN TESTS AND SKIN REACTIONS IN 52 PATIENTS

Diagnosis	Case no.	Precipitin test	Skin reaction
Hashimoto's disease	1–7	+	++
	8	+	+
	9	+	—
	10	—	+
	11	+	—
Primary myxœdema	12	+	++
	13	+	—
	14 and 15	—	+
	16–19	—	—
Thyrotoxicosis	20	+	—
	21–26	—	—
Simple goitre	27–29	—	—
Unclassified	30 and 31	+	++
	32	—	+
Carcinoma of thyroid	33	—	—
Control subjects	34	—	+
	35–52	—	—

Precipitin test: + = positive, — = negative. Skin reactions ++ = strongly positive, + = weakly positive, — = negative

and had a small goitre (case 30). The thyroid-gland uptake of radio-iodine was abnormally low at four and at forty-eight hours after the administration of a tracer dose, but the level of plasma protein-bound iodine at forty-eight hours was at the upper limit of normal. The serum flocculation-tests, which included thymol-turbidity, thymol-flocculation, and colloidal-gold reactions, were normal. In the 2nd patient (case 31) the clinical features and radio-iodine studies suggested thyrotoxicosis, but the serum flocculation-tests were abnormal. Both these patients had precipitating thyroid antibodies as shown by the precipitin test, and they were probably atypical examples of Hashimoto's disease. The 3rd patient (case 32) had been treated for thirty-five years with thyroid extract. She was

TABLE II—RELATIONSHIP OF PRECIPITATING ANTITHYROID ANTIBODIES TO RESULT OF SKIN TESTS WITH SALINE EXTRACT OF THYROID TISSUE

Precipitin test	Skin reaction (no. of cases)		
	Negative (—)	Weakly positive (+)	Strongly positive (++)
Positive	4	1	10
Negative	32	5	0

euthyroid when we saw her, but she gave a history typical of myxœdema before treatment.

Antigen for Skin Testing

A sterile saline extract was prepared from the surgically excised thyroid of a thyrotoxic patient by the method previously described by Goudie et al. (1957). The extract was then passed through a Seitz filter, dispensed in volumes of 0·5–1·0 ml., and stored at −15°C. Samples were cultured under both aerobic and anaerobic conditions at 20°C and 37°C for seven days to ensure sterility.

Skin Tests

The tests were carried out on the volar aspect of the forearms. 32 patients received three intradermal injections: (*a*), containing 0·2 ml. of antigen, (*b*) containing 0·2 ml. of antigen to which had been added 0·05 ml. of a suspension of cortisone acetate ('Cortelan'), and (*c*) containing 0·2 ml. of sterile 0·9% saline solution and 0·05 ml. of cortisone acetate. This procedure was based on the modification of the tuberculin test described by Citron and Scadding (1957). The remaining 20 patients received the first injection only. The tests were read after twenty-four hours, since the reaction was usually maximal at this time. The results were classified as negative (no reaction or an area of erythema of less than 1 cm. diameter), weakly positive (an area of erythema 1 cm. or more in diameter), or strongly positive (an area of erythema 1 cm. or more in diameter with central induration). Because the outline of the skin reaction was irregular, the size of the response was recorded as the mean of the maximum and minimum diameters.

Precipitin Tests

These were performed in all cases on the serum obtained before skin testing, using an agar-diffusion method (Goudie et al. 1957), and also in 38 cases seven to twenty-eight days after the skin test.

Results

The results of the skin reactions in the 52 patients tested are shown in table I. Table II shows that of the 15 patients with positive precipitin tests, 10 had strongly positive skin tests and 1 had a weakly positive reaction. Of the remaining 4 precipitin-positive patients with negative skin reactions, 3 are of special interest. 1 patient with histologically proved Hashimoto's disease (case 9) had an atypical pH-dependent precipitin reaction. The 2nd (case 13), who had primary myœxdema, had a skin reaction which was delayed for forty-eight hours. Because of the criteria laid down, this response was classified as negative. The 3rd patient (case 20) was unequivocally thyrotoxic.

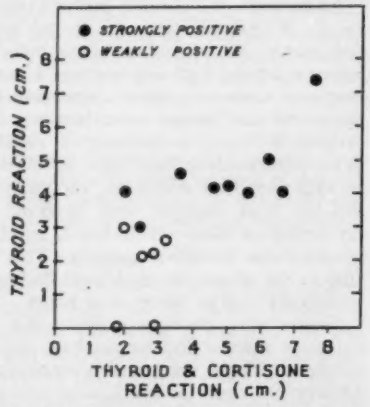


Fig. 1—Comparison of mean diameters of skin reactions to injections of thyroid extract with and without cortisone acetate.

Of the 37 patients with negative precipitin tests, 32 had negative skin reactions and 5 had weakly positive skin reactions (table II). The details of this latter group are as follows. 1 patient (case 10) had had a partial thyroidectomy performed twice previously, and Hashimoto's thyroiditis was diagnosed histologically on the second occasion. After the second operation the patient became myxœdematous, and was treated with thyroxine. Cases 14 and 15 had primary myxœdema; case 32 was unclassified but gave a past history of myxœdema; and case 34, a female of eighty-two years, was 1 of the control series.

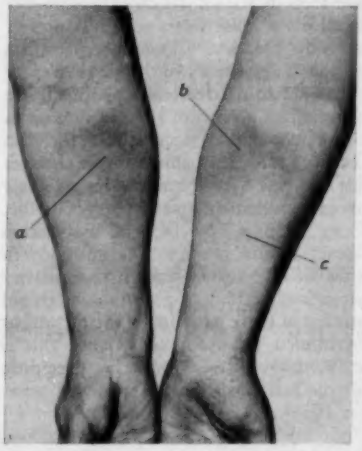


Fig. 2—Skin reactions: (a) strongly positive with antigen alone; (b) strongly positive with antigen plus cortisone; (c) effect of control injection of cortisone acetate in saline.

The effect of adding cortisone to the inoculum was variable.

But there was a tendency for the skin reaction to be enhanced, as is shown in fig. 1 where the mean diameters of the reaction to thyroid extract alone have been plotted against the measurements obtained when cortisone was added. In 2 subjects (cases 11 and 20) a weakly positive reaction was produced with thyroid extract plus cortisone, whereas there was a negative reaction with thyroid alone. In no instance did the intradermal injection of cortisone acetate and saline produce a skin reaction.

An example of a strongly positive response is shown in fig. 2. When indurated, the lesions were often painful and tender. The diameters of the indurated areas varied between 2·5 and 7·25 cm. (average 4·3 cm.), and in those reactions where erythema alone was present the diameters of the lesions were between 1·7 and 3·5 cm. (average 2·5 cm.). Resolution was rapid, being complete in most instances in forty-eight to seventy-two hours. In no case was there vesication, suppuration, or ulceration, and no local sequelæ were observed. An immediate erythematous flare which faded rapidly was noted in several cases, including controls. This bore no relationship to the clinical or serological findings, or to the type of skin reaction at twenty-four hours.

Biopsy of a strongly positive skin reaction showed extensive œdema and hæmorrhage into the dermis and subcutis. There was marked emigration of polymorph neutrophils, many of which were necrotic, together with a few eosinophil leucocytes. Histologically, weakly positive and negative skin reactions were much less extensive, but they were qualitatively similar to the strongly positive reaction. The intradermal injection of 0·2 ml. of 0·9% saline solution, or of an equal volume of an individual's own plasma, produced a similar histological reaction to that following the injection of antigen in a control subject with a negative skin test.

Discussion

Strongly positive skin reactions characterised by both erythema and induration after intradermal injections of human thyroid tissue-extract were seen only in patients with thyroid disease who had precipitating thyroid antibody in the serum. A weakly positive reaction with erythema alone was also seen in 1 such patient. Presumably the skin reaction in all these cases was a manifestation of a local antigen-antibody reaction. This interpretation may also hold for the 5 patients who gave a weakly positive reaction but who had no demonstrable precipitin in the serum; 4 of these had a form of thyroid disease in which precipitins are known to occur, and the 5th (case 34) possibly had latent focal Hashimoto-like changes in the thyroid since she was a euthyroid, elderly female with a positive thyroid complement-fixation test (Goudie, Anderson, and Gray 1958). The lack of association between the skin reaction and precipitating antibody in these cases may thus be due to the known insensitivity of the precipitin reaction. Circulating antibodies might have been demonstrated in these patients by the technique of agglutination of tanned red blood-cells, since this is considered to be more sensitive than the precipitin reaction in Hashimoto's disease and in primary myxœdema (Macgregor 1958).

It is probable, but not certain, that the skin changes seen are those of an Arthus phenomenon. Precipitating antibody is essential for this phenomenon; as shown above, this type of antibody was present in all the patients with strongly positive skin reactions, and it may well have been present even though undetected in those patients showing a weakly positive reaction. The relatively slow development, the macroscopic appearance, and the histological features of the skin response are in keeping with the Arthus phenomenon, but the validity of the histological evidence is doubtful since the control studies using either saline, autologous plasma, or thyroid tissue-extract produced a qualitatively similar, but less marked, microscopic lesion. Preliminary attempts to transmit sensitivity passively to the rabbit have been unsuccessful.

As is shown in fig. 1, the addition of cortisone to the intradermal injection enhanced the skin reaction. Citron and Scadding (1957) observed a similar effect in tuberculin skin-testing, and they suggested that cortisone prolonged the retention of the inoculum at the site of injection, thus increasing the sensitivity of the test. This explanation might also apply to our results, particularly those of the 2 precipitin-positive patients (cases 11 and 20) in whom weakly positive skin reactions developed when cortisone was included in the injection.

This study is, to our knowledge, the first in which local reactions have been observed after the intradermal injection of thyroid extract in patients with spontaneous thyroid disease, though Witebsky et al. (1956) mention a delayed type of skin reaction in rabbits immunised with homologous thyroid tissue. The demonstration of tissue damage at the site of inoculation of thyroid antigen favours the view that some of the changes seen in the thyroid gland in Hashimoto's disease and certain cases of primary myxœdema are the result of an antigen/antibody reaction.

Although the intradermal test may help to elucidate the autoimmune phenomena of human thyroid disease, we believe that it should not be used as a diagnostic test. Effective in-vitro tests are available, and there is a small but appreciable risk of transmitting homologous-serum jaundice by the injection of human thyroid extract. Furthermore, such an injection in a susceptible individual may induce thyroid-antibody formation. Precipitin tests were performed one to four weeks after skin testing in 38 patients, and in 6 of these with thyroid disease changes were observed in the precipitin reaction. In 2 cases of Hashimoto's disease and in a 3rd patient who probably has Hashimoto's disease (case 31) the reaction became weaker or negative. In 1 patient with thyrotoxicosis a weak precipitin reaction developed three weeks after the skin test, but this was no longer present two weeks later. Case 13, with primary myxœdema, and case 20, with thyrotoxicosis, both had weakly positive precipitin reactions which became stronger after the skin test. Unfortunately the significance of the changes in the precipitin reaction in these patients is doubtful, since adequate serial studies to ascertain the constancy of the reaction before skin testing were not made.

Summary

Intradermal tests, using a saline extract of human thyroid tissue as antigen, were carried out in 52 subjects, of whom 33 had thyroid disease. The skin reactions were classified as strongly positive or weakly positive. There was close correlation between the presence of circulating thyroid precipitins and strongly positive skin reactions.

In general, positive skin reactions were observed in patients with Hashimoto's disease or with primary myxœdema. With 1 exception, positive reactions did not occur in individuals without clinical evidence of thyroid disease. The skin reaction was compatible with an Arthus

phenomenon, and the addition of cortisone acetate to the inoculum tended to increase the size of the reaction.

These findings show that thyroid antigen is capable of producing an abnormal tissue reaction in certain patients with thyroid diseases suspected of having an autoimmune ætiology, and they provide a further link between Hashimoto's disease and primary myxœdema.

We wish to thank Dr. J. A. Milne and Dr. S. F. Ferguson Smith for performing the skin biopsies, and Prof. E. J. Wayne for helpful criticism and advice. This investigation was assisted by a financial grant to one of us (J. R. A.) from the Department of Health for Scotland.

REFERENCES

Citron, K. M., Scadding, J. G. (1957) *Quart. J. Med.* **26**, 277.
Goudie, R. B., Anderson, J. R., Gray, K. G. (1958) Unpublished.
— — — Clark, D. H., Murray, I. P. C., McNicol, G. P. (1957) *Lancet*, ii, 976.
Macgregor, A. G. (1958) Personal communication.
Payne, J. R., Terplan, K., Rose, N. R., Witebsky, E., Egan, R. W. (1957) *Surgery*, **42**, 799.
Roitt, I. M., Doniach, D., Campbell, P. M., Hudson, R. V. (1956) *Lancet*, ii, 820.
Trotter, W. R., Belyavin, G., Waddams, A. (1957) *Proc. R. Soc. Med.* **50**, 961.
White, R. G. (1957) *ibid.* p. 953.
Witebsky, E., Rose, N. R., Shulman, S. (1956) *Cancer Res.* **16**, 831.

INOCULATION OF VOLUNTEERS WITH J.H. STRAIN OF NEW RESPIRATORY VIRUS

D. A. J. TYRRELL
M.D. Sheff., M.R.C.P.

M. L. BYNOE
M.B. Lond., D.T.M. & H.

From the Medical Research Council, Common Cold Research Unit, Salisbury, Wilts

MOST mild non-bacterial infections of the respiratory tract, particularly those classified as common colds, cannot be ascribed to any virus which can be cultivated in the laboratory. A virus from a common cold was apparently transmitted in tissue-cultures of human embryo lung, but this experiment could not be repeated and there were no observable changes in the cells of the cultures (Andrewes et al. 1953). It was accordingly of great interest when the recovery of two new viruses named 2060 and J.H. was reported (Pelon et al. 1957, Price 1956). The viruses were found in nasal secretions from cases of mild respiratory illness often resembling the common cold. The two viruses are similar in their general behaviour and are antigenically related but distinguishable (W. J. Mogabgab and W. H. Price, personal communications). It seemed desirable to obtain further data on the multiplication of these viruses in man and on the symptoms they produced. Therefore human volunteers living in strict isolation were inoculated with one of these viruses, and the results are reported here.

Clinical and Laboratory Methods

58 volunteers, aged 18–45 years, were housed, usually in pairs, at this unit and observed as described by Andrewes (1948). Serum was collected on arrival at the unit. At the end of a four-day period of preliminary observation in strict isolation the virus was administered as nasal drops, 0·5 ml. up each nostril. Throat swabs were taken and stored at −60°C in Hanks' saline containing 0·17% bovine plasma-albumin. Nasal washings with Hanks' saline solution were also collected from some volunteers. The volunteers were observed for five days after inoculation, and they sent back further reports of their symptoms and a specimen of serum about a week after leaving the unit.

Monkey-kidney tissue-cultures which had only just spread out into sheets were used. They were grown in either 2% horse serum and Parker's mixture 199 or 4% calf serum and 0·5% lactalbumin hydrolysate in Hanks' saline solution. They were washed once, and, before inoculation, fresh medium was added—either mixture 199 or 0·1% yeast extract and 0·5% lactalbumin in Hanks' saline solution. The latter medium was cheaper than the former and consistently satisfactory, but nevertheless all virus isolations were carried out using medium 199 since Pelon et al. (1957) considered this desirable. All cultures were incubated in a roller drum for ten to fourteen days. All isolations were recognised within a week of inoculation. In later experiments second passages were always done.

The virus used was obtained from Dr. W. Price and had been passed ten times by him in monkey-kidney tissue-cultures. The cytopathic changes described by Pelon et al. (1957) and by Price (1956) were observed when the virus was inoculated in this laboratory, and preliminary studies confirmed many of the observations of Price and Pelon et al. on its other properties.

Neutralisation tests.—About 100 I.D.$_{50}$ of virus were held overnight with serum dilutions. 0·1 ml. of the mixture was inoculated into cultures. Twenty-four hours later the medium was changed. Cultures were observed for up to six days. Virus isolated from throat swabs was identified by a test of this sort carried out with immune sera prepared in rabbits by one intramuscular and two intravenous injections of tissue-culture fluids.

Results

The general results are summarised in fig. 1. In the first two trials tissue-culture fluid from the twelfth passage in monkey-kidney cultures maintained in medium 199 was used. About 100 and 1000 tissue-culture infectious doses (T.C.D.$_{50}$) were given. A few volunteers had mild symptoms, none of which were regarded as indicating a cold, but virus was recovered from the combined nasal washings and throat swabs from each of 2 of the 16 volunteers inoculated. Although ten times more virus was given in trial 2 than in trial 1 the proportion of volunteers infected was no greater. Therefore the infected respiratory secretions from one volunteer in the first trial were diluted 1/6 and used as inoculum in trial 3. In this trial there were two colds—one classified as severe, with hoarseness, cough, and sputum. As in the previous trial, material from this volunteer diluted 1/10 was inoculated to volunteers in trial 4. In trials 3 and 4 four colds occurred in the 20 volunteers inoculated with human-passed virus. Virus was recovered from 3 of the volunteers with colds and from 5 without symptoms. In trials 5 and 6 12 volunteers were inoculated with infected washings from trial 3 which had been mixed with rabbit immune serum (titre 200) as described in the neutralisation test. Control volunteers received a similar mixture of saline solution and serum. One cold was apparently produced by the

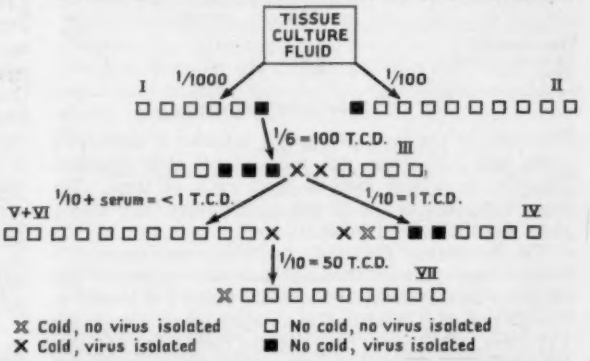


Fig. 1—Summary of results of trials of J.H. virus in volunteers. Next to arrow indicating line of passage is fraction showing dilution of nasal washings and throat-swab fluid used and amount of virus contained in inoculum.

TABLE I—THE LACK OF RELATION BETWEEN THE ANTIBODY TITRE BEFORE INOCULATION AND THE FREQUENCY OF INFECTION AFTER INOCULATION OF J.H. VIRUS

Group of volunteers	No. of volunteers with serum-neutralising antibody (titre)									
	<4	4	8	16	32	64	128	256	>256	<4–>256
Virus isolated ..	3	0	0	1	1	1	0	0	0	6
Virus not isolated ..	9	7	2	5	1	0	0	0	1	25
All	12	7	2	6	2	1	0	0	1	31

mixture of washing and serum, and virus was isolated from washings collected two and four or five days after inoculation. A 1/10 dilution of this washing collected on the second day was given in the final trial. 1 volunteer developed a cold, but no virus was isolated from her throat or from three throat swabs from each of 7 volunteers to whom her nasal washings and throat swabs were passed.

Multiplication of J.H. Virus in the Respiratory Tract

The virus was recovered by nasal washings, nasal swabs, and throat swabs. In the 11 volunteers from whom the virus was recovered it was found in specimens collected on the second to fourth day after inoculation. In 1 volunteer it was found one day after inoculation. Seven specimens were titrated and contained between 50 and 1000 T.C.D.$_{50}$ of virus. In one instance in trial 4 the inoculum contained about 1 T.C.D.$_{50}$, and yet 1000 T.C.D.$_{50}$ was recovered in a swab from 1 volunteer two days later. In other cases the amount of virus recovered was more than 100 times greater than that which had been inoculated. It is therefore certain that the virus multiplies in the nose and throat of man.

Serum Antibody Determinations

The results of antibody titrations are summarised in table I. It is clear that infection occurred in the presence of high levels of circulating antibodies. A rise in antibody titre occurred in 1 laboratory worker who was infected as a preliminary to the trial; otherwise no change in antibody titre was detected in 24 pairs of sera—4 of which came from volunteers from whom virus was isolated.

Relation of Infection by J.H. Virus to Colds

Volunteers infected with J.H. virus often had no symptoms at all, but 4 of 11 of them had typical colds.

TABLE II—THE RELATION BETWEEN THE ISOLATION OF VIRUS AND THE DEVELOPMENT OF COLDS IN VOLUNTEERS RECEIVING VIRUS

Group of volunteers	Number of volunteers who had		Total
	Colds	No colds	
Virus isolated	4 (36%)	7	11
Virus not isolated	2 (4%)	45	47
Total	6	52	58

χ^2 $P < 0{\cdot}01$ (Yates' correction applied).

However, in the later passages 2 volunteers developed colds, and J.H. virus was not isolated after repeated attempts on several samples from each of them. No colds were seen in the 45 other volunteers from whom virus was not isolated (table II).

We thought at first that colds occurred in trial 3 because one passage through man had increased the virulence of the virus; but in trials 4 and 7 it looked as though the colds were due to an agent distinct from the J.H. virus. This might have been an agent lying dormant in the throat of a volunteer in trial 1 which was "activated" by infection with J.H. virus. Alternatively the colds in trial 3 might have been contracted before the trial began. This view would have been supported if volunteers inoculated at the same time with saline solution had developed colds also. 30 such "controls" were included in other trials and none developed colds. None, unfortunately, was inoculated at the same time as trial 3.

J.H. Virus in England

J.H. virus was not isolated from washings from colds in children and adults or, after repeated efforts, from washings containing four different "pedigree" colds at present under study here. It was found that titrations of pools of sera collected in Sheffield about 1955 (fig. 2) suggested that antibody is acquired between infancy and the late twenties, and this correlates with the isolation of the virus in the U.S.A. from children aged 5–15, student nurses, and medical students (W. H. Price, personal communication) and from naval recruits (Pelon et al. 1957).

Discussion

Since we have unequivocal evidence that J.H. virus multiplied in man it is of special interest that some

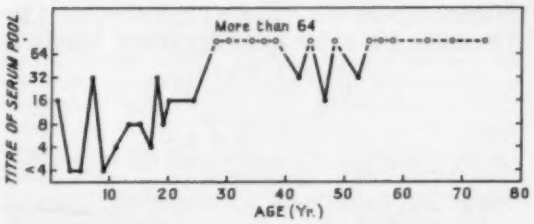


Fig. 2—Levels of neutralising antibody against J.H. virus in pools of sera collected from persons of similar ages. Each pool contains 50 sera from individuals of a 2-year age range (see Davenport et al. 1955).

individuals without antibody were resistant to infection while others with antibody were susceptible, and that no antibody rise was seen in several infected volunteers. Respiratory-virus infections of this type might well fit into the epidemiological pattern of the common cold, but have not previously been observed in man.

These results apparently disagree with those of Pelon et al. (1957) and Price (1956), who demonstrated antibody rises in their patients more often than they isolated the virus. Also Price (1957) states that injection of a killed virus vaccine stimulates antibody formation which protects children against infection and illness induced by J.H. virus. It appears, however, that our virus was different from the "wild" type of virus just isolated from man, in that it grew rapidly in tissue-cultures and in the presence of lactalbumin hydrolysate. It is quite possible that wild virus under natural conditions multiplies more freely than ours does in the nose and throat and can therefore cause obvious illness and an antibody response. A cold virus has been "picked up" before during the passage of a known virus. While attempting to propagate adenovirus type I by serial passage in volunteers A. T. Roden and H. G. Pereira (unpublished) observed a cold in a volunteer from whom adenovirus could not be isolated. This cold was transmitted in series and shown to be unrelated to adenovirus.

The apparent association between J.H. virus and colds in our experiment may be due to the fact that the virus caused symptoms. The association could also have arisen if some volunteers possessed a non-specific resistance against both J.H. virus and another agent which caused

colds, while others were susceptible to both infections. We think that in future trials of this sort interpretation would be easier if a strain was used which had received only a few tissue-culture passages, rather than attempting to readapt to man by serial human passage an apparently attenuated strain.

Summary

88 volunteers took part in experiments with J.H. virus. 58 received the virus and 11 became infected, the virus multiplying in the throat and nose.

Persons with high and low serum-antibody levels became infected, and 12 with low antibody levels escaped infection.

Six colds occurred—four in volunteers infected with J.H. virus and two in volunteers who failed to become infected.

Attempts to isolate the virus from children and adults with colds were unsuccessful, but there is serological evidence suggesting that an antigenically related agent is present in England.

We wish to thank Dr. W. H. Price for supplying the J.H. virus, Miss J. B. Macdonald for help in the clinical observations, and Mr. M. C. Brebner and Mrs. E. Beale for technical assistance. The monkey kidneys and medium 199 used were all kindly supplied by the M.R.C. Poliomyelitis Vaccine Control Laboratories. We are much indebted to the volunteers for their willing and conscientious collaboration.

REFERENCES

Andrewes, C. H. (1948) *J. Royal Soc. Arts*, **96**, 200.
— Chaproniere, D. M., Gompels, A. E. H., Pereira, H. G., Roden, A. T. (1953) *Lancet*, ii, 546.
Davenport, F. M., Hennessy, A. V., Stuart-Harris, C. H., Francis, T., Jr. (1955) *ibid.* ii, 469.
Pelon, W., Mogabgab, W. J., Phillips, I. A., Pierce, W. E. (1957) *Proc. Soc. Exp. Biol., N.Y.* **94**, 262.
Price, W. H. (1956) *Proc. Nat. Acad. Sci., Wash.* **42**, 892.
— (1957) *ibid.* **43**, 790.

MAGNESIUM-LIPID RELATIONS IN HEALTH AND IN PATIENTS WITH MYOCARDIAL INFARCTION

DAVID F. BROWN
M.B. Wales
ASSISTANT IN MEDICINE

ROBERT B. MCGANDY
M.D. Cornell
SENIOR ASSISTANT SURGEON, UNITED STATES PUBLIC HEALTH SERVICE

EDWARD GILLIE
M.D. Albany
RESEARCH FELLOW IN MEDICINE

JOSEPH T. DOYLE
M.D. Harvard
ASSOCIATE PROFESSOR OF MEDICINE

From the Department of Medicine and Cardiovascular Health Center, Albany Medical College, Albany 8, New York

THE possible role of dietary factors in the pathogenesis of atherosclerosis has been widely investigated. Dietary fat has been found to be closely related to this disorder, and the possible relations to it of carbohydrate, protein, vitamins, and trace metals have also been studied.

In the past two years evidence has been accumulating to suggest that magnesium may be involved in atherogenesis. We present here additional data on magnesium-lipid relations and review data on these substances in connection with atherosclerosis.

Malkiel-Shapiro et al. (1956) reported that magnesium sulphate administered parenterally to patients with myocardial infarction produced " clinical improvement ", and that in many instances abnormal serum-lipoprotein levels reverted to normal.

Bersohn and Oelofse (1957) reported significantly higher serum-magnesium levels in Bantu than in Europeans. Bantu are said to have a low incidence of ischæmic heart-disease and lower serum-cholesterol levels than Europeans. In the European group studied, Bersohn and Oelofse claimed to have revealed a strongly negative correlation between serum-magnesium and cholesterol levels.

Vitale et al. (1957b) produced hypomagnesæmia and definite evidence of magnesium deficiency in rats made hypercholesterolæmic by the addition of cholesterol and cholic acid to their diets; dietary magnesium was maintained at levels which were adequate for animals on a normal diet. Previously Hegsted, one of Vitale's coworkers, had concluded that the degree of cholesterol-induced atherosclerosis (manifested by sudanophilia) was proportional to, and probably dependent on, serum-cholesterol levels (Hegsted et al. 1957). Vitale et al. (1957b) greatly diminished or retarded the deposition of lipids in the aorta and heart valves of their animals, on an atherogenic diet, by increasing the dietary magnesium eightfold. Although atherogenesis appeared to be delayed or inhibited by this procedure, the raised serum-cholesterol levels were not depressed, and in some instances were actually raised further. It is thus possible that magnesium may have had some local protective effect on the vessel wall. This view may lend support to that of workers who believe that atherogenesis is more intimately dependent on local factors than on serum-lipid levels.

Magnesium plays a vital role in all organic energy processes (Perry 1956) and is known to be necessary for the action of many enzyme systems (White et al. 1954). Vitale et al. (1957a) have shown that one effect of magnesium deficiency is to uncouple oxidative phosphorylation in heart-muscle mitochondria. Mitochondria are intimately concerned with fatty-acid metabolism; and two laboratories have found uncoupling of oxidative phosphorylation in association with deficiency of essential fatty acid (Klein and Johnson 1954, Tulpule and William 1955). Pyridoxine has been implicated in atherogenesis, and administration of pyridoxine to healthy people is claimed to raise serum-magnesium levels (Buscaino and Balbi 1952).

It seemed to us on experimental and theoretical grounds that magnesium and lipid metabolism, and therefore magnesium and atherosclerosis, might be related. Schroeder (1955) has asked " Is atherosclerosis a conditioned pyridoxine deficiency?"; and there seems to be justification for asking the same question in regard to magnesium.

In the present study possible relations between serum magnesium and certain lipids were investigated in clinically healthy middle-aged American men. The same measurements were carried out on a group of men with recent myocardial infarcts. Serum cholesterol and magnesium were measured in mothers and in their newborn infants because these exhibit an approximately fourfold difference in serum-cholesterol levels; and it was thought that if magnesium and cholesterol levels are related independently of other factors, this relationship would be readily apparent in these two groups.

Material and Methods

Venous blood was obtained from 186 white American men aged 45–59 who were members of the population of approximately 2000 examined annually at the Cardiovascular Health Center at Albany Medical College (Hilleboe et al. 1954). From the group that attended for examination during this study, sera manifesting as wide a range of cholesterol levels as possible were collected and submitted to the further determinations outlined below. Since the subjects were examined at various times throughout the day the sera obtained were not fasting samples. Fasting blood was obtained from 39 patients, in the same age-range as the normal group, on the wards of the Albany Hospital and the Albany Veterans' Administration Hospital, who had been admitted with an acute myocardial infarct. Specimens of

TABLE I—MAGNESIUM-LIPID RELATIONSHIPS IN 186 MIDDLE-AGED MEN

Group no.	Serum-cholesterol range (mg. per 100 ml.)	No. of cases	Mean and standard deviation					
			Cholesterol (mg. per 100 ml.)	Magnesium (mEq. per litre)	Total lipid (mg. per 100 ml.)	α lipid (mg. per 100 ml.)	β-lipid (mg. per 100 ml.)	% α-lipid
1	125–150	4	141 ± 5·2	1·81 ± 0·12	719 ± 187	196 ± 31	523 ± 176	28·3 ± 6·3
2	151–175	8	165 ± 7·5	1·66 ± 0·28	799 ± 134	214 ± 65	583 ± 127	27·0 ± 7·5
3	176–200	25	189 ± 7·5	1·77 ± 0·22	898 ± 153	211 ± 59	691 ± 169	23·9 ± 6·7
4	201–225	26	214 ± 8·1	1·81 ± 0·16	928 ± 107	200 ± 42	723 ± 114	21·9 ± 5·7
5	226–250	24	237 ± 6·7	1·76 ± 0·17	1036 ± 87	210 ± 54	834 ± 110	20·7 ± 6·0
6	251–275	25	260 ± 7·7	1·81 ± 0·23	1084 ± 138	210 ± 59	873 ± 144	19·5 ± 5·6
7	276–300	25	285 ± 6·3	1·86 ± 0·19	1155 ± 117	199 ± 49	962 ± 147	17·5 ± 5·1
8	301–325	25	313 ± 7·7	1·76 ± 0·19	1330 ± 189	220 ± 53	1115 ± 213	17·1 ± 5·0
9	326–350	18	334 ± 7·6	1·86 ± 0·17	1321 ± 151	208 ± 57	1112 ± 203	16·3 ± 5·8
10	351–375	4	364	1·86	—	—	—	—
11	376–400	2	394	1·75	—	—	—	—
12	>400	2	648	1·93	—	—	—	—

TABLE II—MAGNESIUM-LIPID RELATION IN MYOCARDIAL INFARCTION

Serum-cholesterol range (mg. per 100 ml.)	No. of cases	Cholesterol (mg. per 100 ml.)	Magnesium (mEq. per litre)	Total lipid (mg. per 100 ml.)	α-lipid (mg. per 100 ml.)	β-lipid (mg. per 100 ml.)	% α-lipid
134–406	39	246 ± 67	1·81 ± 0·23	816 ± 175	130 ± 61	686 ± 180	16·0 ± 8·0

blood from 20 mothers at term and from the umbilical cord of their infants were obtained from patients on the obstetrical service of the Albany Hospital. In all instances venous blood was obtained, and the withdrawn sera were stored at 4°C. All determinations were carried out within one week of obtaining a specimen.

Serum-cholesterol was measured by the method of Abell et al. (1952). Total lipids were estimated by a modification of the micro-method of Swahn (1953), and lipoprotein distribution by the method of Jencks and Durrum (1955). Absolute values for α and β lipoprotein lipid were obtained by multiplying figures for total lipid by the percentage α and β lipoprotein obtained by paper electrophoresis. Serum-magnesium levels were measured by the method of Orange and Rhein (1951) using a 5 cm. cuvette in a Beckman DU spectrophotometer.

Results

The results are shown in table I. Serum magnesium and lipid values for men with recent acute myocardial infarction are presented in table II. The mean serum-cholesterol value in the 20 females at term was found to be 273 ± 52 mg. per 100 ml., whereas that in the cord blood of the newborns was 82 ± 17 mg. per 100 ml. The mean serum-magnesium level in the mothers was 1·49 ± 0·2 mEq. per litre, and in the newborns 1·55 ± 0·2 mEq. per litre. The difference between these mean magnesium levels is not significant, while that between the cholesterol levels is highly so.

Discussion

It is apparent from table I that the mean cholesterol value increases in each group, from a value of 141 mg. per 100 ml. in group 1 to 648 mg. per 100 ml. in the final group. It is also apparent that there is no consistent trend in the mean magnesium levels. Statistical evaluation revealed that there is no correlation between magnesium and cholesterol levels. Coincident with the group increase in serum-cholesterol levels there is a progressive increase in total serum-lipid values from a minimum of 719 mg. per 100 ml. in group 1 to 1321 mg. per 100 ml. in group 9. Values for lipids other than cholesterol were not obtained for groups 10–12. When values for α and β lipoprotein lipid, which comprise total lipid, are inspected, it is seen that the increase in total lipid is accounted for almost entirely by an increase in the lipid content of the β-lipoprotein fraction.

As with cholesterol, no correlation was found between magnesium and any of the other lipid elements measured. The fourfold difference in cholesterol levels between mother and child was not associated with significantly different magnesium levels. In none of our groups, therefore, can we confirm the observation of Bersohn and Oelofse (1957) of an inverse relation between magnesium and cholesterol.

Because of the arbitrary method of selection of the 186 subjects in the healthy group, no direct comparison of their various serum values with those of the infarct group can be made. The mean serum-cholesterol value of 246 mg. per 100 ml. in the infarct group may be considered normal, and approximates the mean value of 237 mg. per 100 ml. for the clinically normal individuals in group 5 of table I. The mean serum-magnesium level of 1·81 mEq. per litre in the infarct group may also be considered normal as it differs little from the mean values obtained in the healthy groups.

Although this study reveals no correlation between serum-magnesium levels and serum-lipids, and no significant difference between serum-magnesium in normal individuals and in those with myocardial infarction, the role of magnesium in ischæmic heart-disease cannot be completely discounted. Fitzgerald and Fourman (1957) have shown that persons on a low-magnesium diet maintain normal serum-magnesium levels. However, in contradistinction to persons on a normal magnesium diet who will excrete almost 100% of a parenterally-administered dose of magnesium sulphate (Smith et al. 1942) the subjects studied by Fitzgerald and Fourman (1957) retained 25–42% of such a dose. In other words, negative magnesium balance can exist in the presence of normal serum-magnesium levels. We hope to study the urinary excretion of parenterally administered magnesium in normal and in atherosclerotic persons. Malkiel-Shapiro (1956) stated that salts of magnesium are useful in ischæmic heart-disease, but included no statistical evaluation of his findings. It would seem advisable that further work designed to assess the therapeutic value of magnesium in ischæmic heart-disease should be carried out by a double-blind procedure.

Conclusions and Summary

Recent work has suggested that magnesium may be related to atherosclerosis and ischæmic heart-disease. It has been claimed that magnesium sulphate is of therapeutic value in myocardial infarction, while a high-magnesium diet has prevented the development of atherosclerosis in rats. A strongly negative correlation between serum-magnesium and serum-cholesterol levels has previously been reported.

In the present study serum-magnesium, cholesterol, and lipoprotein lipid were measured in clinically healthy middle-aged white American men exhibiting a wide range of cholesterol and lipid values. These determinations were also carried out on a similar but smaller group with recent myocardial infarction. No correlation was found between serum-magnesium and any of the lipid entities measured. While α-lipoprotein lipid in the infarct group was considerably lower than in the normal group, no difference in the magnesium levels was noted. No difference in magnesium levels was found between 20 mothers and their newborn infants, who exhibited a four-fold difference in their cholesterol levels.

Although the present study has yielded no evidence of any relation between serum-magnesium and lipids, this does not exclude the possibility that magnesium has a role in the pathogenesis of atherosclerosis.

REFERENCES

Abell, L. L. Levy, P., Brodie, B., Kendall, F. (1952) *J. biol. Chem.* **195**, 357.
Bersohn, I., Oelofse, P. J. (1957) *Lancet*, i, 1020.
Buscaino, V. M., Balbi, R. (1952) *Boll. Soc. ital. Biol. sper.* **28**, 113.
Fitzgerald, M. G., Fourman, P. (1957) *Clin. Sci.* **15**, 635.
Hegsted, D. M., Andrus, S. B., Gotsis, A., Parkman, O. (1957) *J. Nutr.* **63**, 273.
Hilleboe, H. E., James, G., Doyle, J. T. (1954) *Amer. J. publ. Hlth.* **44**, 851.
Jencks, W. P., Durrum, E. L. (1955) *J. clin. Invest.* **34**, 1437.
Klein, P. D., Johnson, R. M. (1954) *J. biol. Chem.* **211**, 103.
Malkiel-Shapiro, B., Bersohn, I., Terner, P. E. (1956) *Med. Proc.* **2**, 455.
Orange, M., Rhein, H. C. (1951) *J. biol. Chem.* **189**, 379.
Perry, S. V. (1956) *Physiol. Rev.* **36**, 1.
Schroeder, H. A. (1955) *J. chron. Dis.* **2**, 28.
Smith, P. K., Winkler, A. W., Hoff, H. E. (1942) *Anesthesiology*, **3**, 323.
Swahn, B. (1953) *Scand. J. Lab. clin. Invest.* **5**, suppl. 9.
Tulpule P. G., William, J. N., Jr. (1955) *J. biol. Chem.* **217**, 229.
Vitale, J. J., Nakawara, M., Hegsted, D. M. (1957a) *ibid.* **228**, 573.
— White, P. L., Nakawara, M., Zamchek, N., Hellerstein, E. E. (1957b) *J. exp. Med.* **106**, 757.
White, A., Handler, P., Smith, E. L., Stetten De W., Jr. (1954) Principles of Biochemistry. New York.

PHENYLBUTAZONE IN THE TREATMENT OF TEMPORAL ARTERITIS

S. E. BJÖRKMAN
M.D. Lund

LECTURER IN MEDICINE, UNIVERSITY OF LUND

From the Department of Medicine, Malmö General Hospital, Sweden

TEMPORAL arteritis, a vascular disease of unknown ætiology, has been diagnosed with increasing frequency during the past ten years. In 1954 Roux was able to trace 248 reported cases. The disease is now so widely known that single case-reports are no longer published. Pathological evidence indicates that the syndrome is a local manifestation of a generalised arterial disease (Cooke et al. 1946, Cardell and Hanley 1951, Heptinstall et al. 1954). The severe local symptoms are due to affection of the temporal and ophthalmic arteries, but the conspicuous general symptoms suggest that the disease is by no means limited to these regions.

The natural course of the disease is characterised by gradual recovery within months or years. Apart from occasional sudden blindness, which is usually bilateral, the prognosis is good, though a case-mortality of 10% of patients with manifestations of giant-cell arteritis has been reported.

Since 1950 treatment with corticotrophin or corticosteroids has been generally accepted as the most effective, and has usually produced prompt relief. Such treatment, however, apparently has no appreciable influence on the progress of the underlying pathological changes, for biopsies during follow-up show no signs of regression. Withdrawal of corticotrophin or corticosteroids is not infrequently followed by recurrences, and long-term treatment is therefore recommended (Birkhead et al. 1957).

Between 1951 and 1957, 14 cases of temporal arteritis were treated in the Department of Medicine, Malmö General Hospital. 8 of these, admitted during 1954 or later, were treated with phenylbutazone ('Butazolidine') instead of corticotrophin or corticosteroids. We were prompted to use this preparation because of its favourable effect on a patient with temporal arteritis who had relapsed during treatment with cortisone (case 3), and also because of the remarkably rapid recovery of patients with another painful vascular disease—namely, superficial thrombophlebitis—during treatment with phenylbutazone. In 7 of the 8 cases of temporal arteritis treated with phenylbutazone there was a good therapeutic effect, and as yet no recurrences have been seen. 1 patient had no symptoms. The relief is thought to be due, at least in part, to regression of concomitant thrombophlebitis in the temporal vein.

Case-reports

Case 1.—A woman, aged sixty-six, had had attacks of migraine for the past forty years, and diffuse rheumatic pain in the knees and shoulder-joints for several years. Recently she had also had attacks of dizziness; during such an attack on July 17, 1955, she sustained a blow against her right temple. Since then she had had continuous right-sided headache and had felt weak. She had lost over a stone in two months. On Aug. 31 she was admitted to another hospital. Both temples were swollen and tender, she had leucocytosis, and the erythrocyte-sedimentation rate (E.S.R.) was increased.

On Sept. 4 the patient was transferred to the department of medicine, Malmö General Hospital, where biopsy of a branch of the right temporal artery showed the typical picture of giant-cell arteritis. After forty-eight hours' treatment with phenylbutazone 0·2 g. t.i.d. she was afebrile and symptom-free. Treatment was continued for fourteen days, and the symptoms did not recur on withdrawal. Her general condition improved, and follow-up examination three months later revealed no abnormality except an E.S.R. of 100 mm. in the first hour (Westergren).

Case 2.—A woman, aged seventy-two, had moderate diabetes mellitus not requiring insulin. The right lower leg had been amputated in 1950 because of gangrene in the foot. At the end of 1955 she had had an attack of rotatory vertigo. She had also noticed some tender spots in front of her right ear. Just before admission on Jan. 2, 1956, pain also developed in the left temple.

On admission to the medical department she had high fever, and both temples were extremely tender to palpation. Temporal arteritis was diagnosed (without biopsy) and she received phenylbutazone 0·2 g. t.i.d. The pain disappeared after twenty-four hours' treatment, and after a further three days she was afebrile. Treatment was continued for fourteen days. There was no relapse on withdrawal. The patient died in the spring of 1958. At necropsy the vessels were carefully scrutinised. The temporal arteries were of normal histological appearance, but a small branch of the abdominal aorta showed atheromatous changes and also hyaline fibrosis of the media. This was regarded as a scar from earlier arteritis (Prof. F. Linell).

Case 3.—A woman, aged sixty-five, had had several spells of mental depression between 1946 and 1948, but she had not received electroconvulsive therapy. In 1953 auricular fibrillation was diagnosed. In 1954 she was admitted to a mental hospital because of further depression. The E.S.R. at that time was 10 mm. in the first hour. A month after she was discharged from hospital left-sided headache developed, with tenderness of the left temple.

On admission to Malmö General Hospital on May 8, 1954, the patient was febrile and had excruciating headache, with tenderness over both temples. The skin was red and swollen,

and the temporal arteries were tender to palpation, but their pulsations could be easily felt. Biopsy showed giant-cell arteritis. Treatment was started with cortisone 100 mg. daily, which was later reduced to 25 mg. She recovered rapidly, and three weeks later she was sent home on a maintenance dose of cortisone, 25 mg. per day. Her E.S.R. had then decreased from 100 mm. to 21 mm. in the first hour.

After a few days at home the headache recurred and there was a slight increase in temperature. She also complained of diffuse pain in the back and both arms. She was readmitted to the medical department. The temples were no longer tender. This time cortisone failed to produce any relief or to lower her temperature. After a month cortisone was replaced by phenylbutazone, 0·2 g. t.i.d. Five days later the pain had disappeared and the temperature was normal. Treatment was continued for eighteen months, but with a smaller dose during the last twelve months. The E.S.R. did not return to normal until she had been treated for a year. When she was last seen, in February, 1958, her general condition was good.

Case 4.—A man, aged seventy-six, had previously always had good health. On Dec. 26, 1955, the right eye suddenly went blind, and on Jan. 9, 1956, the left was also affected. He was afebrile, but the E.S.R. was increased. Both temporal arteries felt normal, but biopsy of the left artery showed typical giant-cell arteritis. From Jan. 12 he received phenylbutazone 0·2 g. t.i.d., but after eleven days' treatment he was still blind. He was therefore given a large dose of cortisone without any recovery of vision, and this treatment could not be continued for long because he became mentally confused, with hallucinations. When last seen a year later, he was still blind but otherwise felt well.

Case 5.—A woman, aged sixty-five, had an uncomplicated myocardial infarction in 1955. In September, 1956, she had pain in the back of her head, which responded well to X-ray therapy. In November of that year she had a cold, and the pain returned. In February, 1957, she had diffuse rheumatic pain which was not localised to the joints. She had lost nearly a stone in six months. She was found to have an E.S.R. of 80 mm. in the first hour, but other investigations failed to reveal any explanation for the symptoms.

Since the menopause, at the age of forty-eight, she had had attacks of headache accompanied by teichopsia. In the middle of May, 1957, she began to feel continuous pain of a different type over the right eye. She was again admitted to hospital, this time because of a suspected brain tumour, but this could not be confirmed. Her temporal arteries felt normal.

When she was seen later (as an outpatient) a tender spot was palpated over her right temporal artery. She was given a course of phenylbutazone for only three days. Although she had had headache almost continuously for four months, it now disappeared and did not return. During this treatment 3 red granulomas appeared, all pea-sized, and localised to the temporal artery. They were not tender. Biopsy was not done.

Case 6.—A man, aged fifty-eight, had always been in good health. Three weeks before admission he began to feel pain in the right temple, which made the wearing of a hat uncomfortable.

On admission to the medical department an elevated, tender spot was observed over the right temporal artery. The E.S.R. was 47 mm. in the first hour. Three days' treatment with phenylbutazone produced complete relief; but this was continued for a month, during which the E.S.R. decreased to 10 mm. in the first hour. There was no biopsy.

Case 7.—A man, aged sixty-three, had always been in good health. In the middle of April, 1957, he had severe headache localised mainly to his left temple. On May 20 he became febrile, and he was admitted to the otological department because of suspected brain abscess or sinus thrombosis. His E.S.R. was 96 mm. in the first hour. The tentative diagnosis could not be confirmed. He was therefore transferred to the medical department, where he remained a diagnostic problem. His temporal arteries felt normal. Cerebral angiography revealed no signs of a pathological condition. The possibility of temporal arteritis was considered, and he was given a course of phenylbutazone. Within two days he was afebrile and his pain disappeared. After five months the E.S.R. was normal. No biopsy was done.

LABORATORY DATA IN 8 CASES OF TEMPORAL ARTERITIS

Case no.	Hb (%)	E.S.R. (mm. in 1st hr.)	White blood-cells (per c.mm.)	Fibrinogen (g. per 100 ml.)	Electrophoresis (g. per 100 ml.)	
					α_2 globulin	γ-globulin
1	68	137	8000	0·90	1·20	1·26
2	58	145	11,000	0·90	1·33	1·52
3	64	112	9600	0·70	0·87	1·0
4	90	50	11,000	..	..	..
5	89	40	6200	0·50	0·58	1·38
6	93	73	5800	..	..	..
7	86	100	10,000	0·70	0·89	1·03
8	57	57	11,800	..	..	..

Case 8.—A man, aged fifty-nine, had had rheumatoid arthritis since 1932. In 1954 severe albuminuria and decreased serum-albumin were noted, and were thought to be signs of renal amyloidosis. On Dec. 27, 1957, the left temple became swollen and tender, the patient was feverish and complained of headache. Two cords the thickness of a pencil and about 4 cm. long were felt along the course of the temporal artery. After two days' observation he was given phenylbutazone for only two days. Both the pain and the swelling disappeared promptly. He suddenly died a month later from profuse gastric hæmorrhage. At necropsy phlebitis was found in the left temporal vein, but the artery was normal. Widespread amyloidosis was also found (Prof. F. Linell).

Comment

The diagnosis of temporal arteritis was verified by biopsy in 3 cases, and in a 4th temporal phlebitis was found at necropsy a month after signs of the temporal syndrome had appeared. In a 5th case necropsy two years after the acute onset revealed healed lesions in a branch of the abdominal aorta. In the other cases the diagnosis was made on clinical grounds. In cases 1–4 and 7 the symptoms were typical, but they were less so in cases 5, 6, and 8.

Case 4 is remarkable in that the patient had no temporal symptoms despite a typical picture of arteritis at biopsy, which was done because of sudden blindness, nor did any signs appear later. In case 3 cortisone produced a prompt response; but later, when the dose was reduced, the clinical picture deteriorated, probably because of the arteritis.

Phenylbutazone invariably controlled the pain and fever. The general condition usually improved also, so that the patient could soon leave hospital. No side-effects or relapses were seen. The increased E.S.R. was not influenced by the treatment. In 1 case in which the patient had become blind, eleven days' treatment failed to produce any improvement of vision.

Discussion

The general symptoms of temporal arteritis are loss of weight, diffuse rheumatic pain, and fever; and they are associated with leucocytosis, increased E.S.R., and increased plasma-fibrinogen. The electrophoretic pattern of the serum is abnormal, with a strikingly increased α_2 fraction (see accompanying table). These changes often precede the local symptoms and persist after the latter have disappeared. But it is the temporal symptoms that usually suggest giant-cell arteritis, which might otherwise hardly be suspected. In this respect the local symptoms resemble the butterfly erythema in disseminated lupus erythematosus, or the cutaneous sarcoid in generalised sarcoidosis. Hence the importance of a careful examination of the temples in elderly people with puzzling symptoms.

Phenylbutazone has not been used before for temporal arteritis. We found it to be effective; both the fever and the pain disappeared as rapidly as when steroids are used,

and there seems to be little risk of relapse. The response to phenylbutazone resembles that of superficial thrombophlebitis (Stein and Rose 1954) though it is more rapid and more permanent.

Phlebitis in the temporal vein has been reported by Crosby and Wadsworth 1948, and by Peet 1951. Eckerström (1946) described 3 cases in which only the vein was believed to be affected. In 1 of these histological examination of the venous wall showed changes resembling those in affected arteries though the accompanying artery was unfortunately not examined histologically. Case 8 here bears some resemblance to this case in that thrombophlebitis was the only finding at necropsy. The situation might have been similar in case 6, where the course of the disease was short.

In temporal arteritis a vein is seldom removed for microscopic examination. But without biopsy it is not always easy to decide whether the tenderness to palpation of the temple is due to a granuloma in the wall of the artery or to phlebitis in the adjacent vein. Swelling and reddening of the skin in the temporal region are typical signs of thrombophlebitis. Case 4 illustrates that an inflammatory process in the artery does not always produce temporal pain. Crosby and Wadsworth (1948) have shown that the inflammation spreads from the artery to adjacent veins. Because of their superficial course and the underlying hard bone, the temporal vessels are also particularly susceptible to trauma, which might favour phlebitis. One is tempted to assume that the phlebitis is responsible for the clinical symptoms of temporal arteritis. Should this assumption be correct, the response to phenylbutazone would be comparable to that seen in superficial thrombophlebitis elsewhere.

The agonising headache of temporal arteritis has been ascribed to compression of nerves running through tissue in which there are granulomatous changes. But the headache may be of vascular origin. The role played by the temporal vessels as a cause of headache is illustrated in migraine. Œdema, as seen in temporal arteritis, may also contribute to pain if it is localised to the tight connective tissue of the galea. The known antiphlogistic property of phenylbutazone might counteract this inflammatory œdema and thereby relieve the pain.

The fact that phenylbutazone produces no demonstrable effect on the increased E.S.R. or on the electrophoretic serum pattern indicates that treatment is purely symptomatic. In view of the striking effect of the drug on thrombophlebitis, however, a possible direct action on the inflammatory process in the vessel wall can hardly be denied. In cases with pronounced general symptoms, it therefore seems advisable to continue treatment longer in the hope that healing might be promoted.

Obscure cranial symptoms are often encountered within the age-group in which temporal arteritis is most common. When there are general symptoms, the possibility of cancer must also be considered. In such cases the prompt effect of phenylbutazone may be of differential-diagnostic value, as in 1 of the cases reported above.

Summary

8 cases of temporal arteritis are described in which treatment with phenylbutazone gave rapid relief from symptoms.

There was no recurrence on withdrawal. The effect is comparable to that obtained with corticotrophin or corticosteroids.

References at foot of next column

AMMONIA INTOXICATION FOLLOWING URETEROSIGMOIDOSTOMY IN A PATIENT WITH LIVER DISEASE

REUBEN SILBERMAN
M.B. W'srand, F.R.C.S., F.R.C.S.E.

From the Urologic Service of the Department of Surgery, Memorial Center for Cancer and Allied Diseases, New York, U.S.A.

RAISED blood-ammonia levels are commonly associated with the neurological changes of liver failure (Phear et al. 1955). These changes give rise to the clinical syndrome of " ammonia intoxication " or " hepatocerebral intoxication ". In the following case the patient, who had a cirrhotic liver, developed ammonia intoxication after ureterosigmoidostomy. A similar case has been previously described (McDermott 1957).

Case-report

The patient, a housepainter aged 61, was admitted under the care of Dr. Willet Whitmore on Nov. 28, 1957.

History

He said that he had been treated elsewhere for " bladder tumours ". During the previous nine years he had had approximately 24 cystoscopic examinations and treatments and 2 suprapubic operations. His complaints on admission were progressive hæmaturia, frequency, and dysuria. There was no past history suggesting liver disease or alcoholism.

Examination and Investigations

The patient appeared healthy. His blood-pressure was 170/120 mm. Hg. The only abnormalities noted were a just palpable liver edge, and mild prostatic enlargement.

Cystoscopy showed that the bladder capacity was reduced to 30 ml.: the mucosa was reddened and scarred. Biopsy of a suspicious area, and a subsequent deep-muscle biopsy under general anæsthesia, were negative for carcinoma; but malignant cells were found in the urine. Radiological and laboratory investigations were otherwise normal.

Operation

In view of the history of multiple recurrent tumours, increasingly severe symptoms with a much reduced bladder capacity, and the malignant cells in the urine, the patient was submitted to a radical cystectomy and bilateral ureterosigmoid anastomoses. For the anastomoses Leadbetter's technique was used (Leadbetter 1951). The patient was opposed to an ileal bladder because he did not wish to have an opening on his abdominal wall. At operation a nodular, firm cirrhotic liver was noted: its size was about half to a third of normal. The abdominal wall was closed with interrupted figure-of-eight steel-wire sutures, incorporating peritoneum, muscle, and rectus-sheath, and with subcutaneous and skin sutures.

Microscopic examination of the operation specimen showed a superficially infiltrating papillary epidermoid carcinoma (grade II) of the bladder and a carcinoma-in-situ of the left ureteric stump. The lymph-nodes were free of disease.

Postoperative Complications

Postoperatively the patient was maintained on gastric suction and intravenous fluids, and a rectal tube was inserted for urinary drainage. Initial recovery was uneventful, except for low-grade pyrexia and weakness, and by the seventh postoperative day he was eating a normal diet. On the ninth post-

DR. BJÖRKMAN: REFERENCES

Birkhead, N. C., Wagener, H. P., Shick, R. M. (1957) *J. Amer. med. Ass.* **163**, 821.
Cardell, B. S., Hanley, T. (1951) *J. Path. Bact.* **63**, 587.
Cooke, W. T., Cloake, P. C. P., Govan, A. D. T., Colbeck, J. C. (1946) *Quart. J. Med.* **15**, 47.
Crosby, R. C., Wadsworth, R. C. (1948) *Arch. intern. Med.* **81**, 431.
Eckerström, S. (1946) *Acta med. scand.* **170**, suppl. p. 169.
Heptinstall, R. H., Porter, K. A., Barkley, H. (1954) *J. Path. Bact.* **67**, 507.
Peet, R. M. (1951) *Irish J. med. Sci.* **6**, 387.
Roux, J.-L. (1954) *Helv. med. acta*, suppl. p. 34.
Stein, I. D., Rose, O. A. (1954) *Arch. intern. Med.* **93**, 899.

operative day, however, he developed partial wound dehiscence. This was immediately repaired under general anæsthesia with through-and-through silver-wire sutures, and he was put back on continuous gastric suction and intravenous fluid replacement for another three days. He also received intramuscular injections of chloramphenicol, 2 g. daily, for five days, followed by nitrofurantoin ('Furadantin'), 100 mg. three times a day, for eight days. In spite of this he continued to run a low-grade fever. Because his hæmoglobin was 10·2 g. per 100 ml. he was given 1500 ml. blood over the second, third, and fourth days after the second operation.

On the fourth day after the repair the patient developed jaundice. His serum-bilirubin was 2·25 mg. per 100 ml.; and the total serum-proteins were 7·5 g. per 100 ml. (serum-albumin 3·1 g.). At the same time he developed œdema of the legs and genitalia. There was no calf tenderness. Intravenous fluids were discontinued, and he was given intramuscular meralluride *U.S.P.* ('Mercuhydrin') 2 ml. and intravenous salt-poor human serum-albumin, 50 g. Within three days both the œdema and the jaundice had cleared. At this time the total serum-proteins were 6·7 g. per 100 ml. (serum-albumin 2·8 g.) the blood-urea nitrogen was 13·9 mg. per 100 ml., the serum-chlorides were 105 mEq., and the serum-CO_2 19 mEq. per litre. On the eleventh day after the second operation the patient had anorexia and nausea; and he vomited 100 ml. On the morning of the thirteenth day he was disorientated and restless; and by the afternoon he became stuporose. He then developed profuse diarrhœa, hyperventilation, and bilateral extensor plantar responses. Examination of the blood showed: ammonia, 350 μg. per 100 ml.; pH, 7·55; serum-CO_2, 14 mEq. per litre; serum-potassium, 4·51 mEq. per litre; and blood-urea nitrogen, 18·2 mg. per 100 ml. These findings confirmed the diagnosis of ammonia intoxication with respiratory alkalosis.

Treatment and Progress

An intravenous infusion of 1000 ml. 5% dextrose-in-water, containing 50 g. arginine glutamate and 40 mEq. potassium, was started. The patient was also given intramuscular erythromycin, 300 mg. six-hourly.

Within four hours his condition improved dramatically: he became almost fully conscious, the plantar responses became flexor, and the diarrhœa ceased. Over the ensuing twelve hours he received a further intravenous infusion of 500 ml. 5% dextrose-in-saline, 1000 ml. 5% dextrose-in-water, and 60 mEq. potassium.

On the following day he was fully orientated and afebrile; and physical examination was negative. A rectal tube provided adequate drainage of urine after the diarrhœa had ceased. He was given a liquid, low-protein diet, a multiple-vitamin preparation, sulphafurazole ('Gantrisin'), 1 g. three times a day, and neomycin, 250 mg., twice daily. Erythromycin was discontinued. He received a supplement of 2500 ml. intravenous fluids daily for three days.

The blood-ammonia two days after the intoxication was 180 μg. per 100 ml.; the blood-pH was 7·43; the serum-CO_2 21·8 mEq.; the serum-sodium 132 mEq.; and the serum-potassium 4·68 mEq. per litre; the blood-urea nitrogen was 12·6 mg., and the total serum-proteins 7·2 g. per 100 ml. Clinical progress was maintained without interruption; and his protein intake was gradually increased to 60 g. per day.

Condition on Discharge

When the patient left hospital his rectal control was good; he voided three times at night, and every one or two hours during the day. The wound was healed. His blood-urea nitrogen was 5·0 mg. per 100 ml.; the serum-chloride was 118 mEq., and the serum-CO_2 16 mEq. per litre. An intravenous pyelogram showed normal function and outline. He was given a 60-gramme protein diet, and he was told to maintain a good fluid intake. Neomycin 250 mg. daily and sulphafurazole, 1 g. three times a day, were also prescribed. In view of the raised chloride and depressed carbon-dioxide levels it was felt that he might require salt-restriction and sodium bicarbonate, and his doctor was advised accordingly.

Discussion

Ammonia is present in the peripheral bloodstream in a concentration of less than 90–100 μg. per 100 ml. (Roberts et al. 1957). It arises from the intracellular catabolism of aminoacids and muscle adenine and also from the action of enzymes and bacteria on the intestinal contents (Sherlock 1955). Under normal conditions most of it combines with glutamic acid to form glutamine, a detoxication mechanism (Riddell 1955). Ammonia which reaches the liver enters the Krebs ureacycle and is converted to urea.

Blood-ammonia levels may be raised when there is impaired liver function, with or without portosystemic shunts. Further elevation may result from diversion of the urinary stream to the intact colon. This provides additional ammonia for absorption, especially when there is stasis of urine in the colon (Mitchell and Valk 1953, Mathisen et al. 1957). In the absence of liver dysfunction this additional load can be adequately dealt with by the liver; and the peripheral blood-ammonia level does not rise (McDermott 1957). A damaged liver, however, may be unable to metabolise even a normal amount of ammonia; and the extra load produced by ureterosigmoidostomy will then lead to a corresponding rise in the peripheral blood-ammonia level.

In our patient, a cirrhotic, the liver reserve was low from the outset: no doubt this was partly responsible for the poor wound healing. The stress of the cystectomy and of the postoperative complications must have caused further liver damage: this is suggested by the jaundice and the fall in the serum-albumin level. It is possible to account for the ammonia intoxication on these grounds alone, without postulating excessive ammonia absorption from the colon; but it is reasonable to assume that the additional load of ammonia was a not unimportant causative factor.

Theoretically diversion of the urinary stream to an ileal bladder appears less hazardous than ureterosigmoidostomy. An ileal bladder does not provide as large a reservoir for urinary stagnation and for ammonia absorption as does the entire colon; and because it is less liable to infection than is the urinary tract after ureterosigmoidostomy, there is a smaller likelihood of bacterial decomposition and of ammonia formation. Had our patient not refused, an ileal bladder would probably have been preferable in his case, though the only similar case previously reported was a patient with an infected ileal bladder (McDermott 1957).

An associated feature of the ammonia intoxication in our patient was the respiratory alkalosis. Roberts et al. (1956) observed that in hepatic dysfunction this was more common than metabolic acidosis: it is possibly due to the enhanced respiration caused by ammonia.

Our patient responded well to treatment. Though his recovery may have been partly spontaneous, aided perhaps by the onset of diarrhœa, a further trial of arginine glutamate may be worth while.

The patient was clinically well on discharge; but his serum-chloride level was still raised and his CO_2-combining-power was depressed, indicating a tendency towards hyperchloræmic acidosis. His low blood-urea nitrogen was thought to show a poor liver reserve. He was started on high fluid intake and sulphafurazole to prevent urinary infection, which might precipitate clinical hyperchloræmic acidosis: and a low-protein diet and neomycin were prescribed against recurrence of the ammonia intoxication.

Summary

A cirrhotic patient underwent cystectomy and ureterosigmoidostomy. Postoperative complications culminated in ammonia intoxication with respiratory alkalosis. He responded well to treatment which included arginine glutamate.

Urinary diversion to the colon was probably partly responsible for the ammonia intoxication. In the presence of liver disease an ileal bladder may be a less hazardous alternative.

I should like to thank Dr. Willet Whitmore for permission to publish this case and also for his valuable advice and criticism in the preparation of the paper. Thanks are also due to the staff of the André and Bella Meyer Physiology Laboratory for the estimations of blood-ammonia and pH, and to Dr. I. R. Mendelson for help in preparation of the paper.

REFERENCES

Leadbetter, W. F. (1951) *J. Urol., Balt.* **65**, 818.
McDermott, W. V. (1957) *New Engl. J. Med.* **256**, 460.
Mathisen, W., Whitmore, W. F., Randall, H. T., Roberts K. E. (1957) *J. Urol.* **77**, 27.
Mitchell, A. D., Valk, W. L. (1953) *ibid.* **69**, 82.
Phear, E. A., Sherlock, S., Summerskill, W. H. J. (1955) *Lancet*, i, 836.
Riddell, A. G. (1955) *Ann. R. Coll. Surg. Engl.* **17**, 319.
Roberts, K. E., Thompson, F. G., Poppell, J. W., Vanamee, P. (1956) *J. appl. Physiol.* **9**, 367.
Sherlock, S. (1955) Diseases of the Liver and Biliary System. Oxford.

THE CARDIORESPIRATORY SYNDROME OF EXTREME OBESITY

G. M. BERLYNE
M.B. Manc., M.R.C.P.
RESIDENT MEDICAL OFFICER, MANCHESTER ROYAL INFIRMARY

THE syndrome of polycythæmia, cyanosis, and excessive obesity, though rare, has been increasingly recognised in the United States. In the only well-authenticated case reported in this country the patient died (Counihan 1956). The following case shows the specifically curative effect of a low-calorie diet.

Case-history

An unmarried 42-year-old foreman was admitted, as an emergency, to the Manchester Royal Infirmary on Jan. 1, 1958, complaining of shortness of breath. Though he had been overweight since the age of 7, he had been able to take part in competitive sports both at school and as a young man: he had played amateur football and had been a keen swimmer. He weighed 17 st. at the age of 20 and 20 st. at 25: his maximum recorded weight was about 26 st.

Throughout life he had enjoyed an enormous appetite; and he admitted that, besides eating to excess, he was addicted to alcohol; for many years he had been drinking up to sixteen pints of beer every evening.

Despite his increasing weight he had kept well until a few years ago, when he began to notice that he was becoming more and more short of breath. About six months before admission walking a hundred yards made him dyspnœic; six weeks before admission he was unable to walk even this distance; and for the last few days he felt as though he could hardly breathe, even at rest. He was more comfortable reclining on the right side than when sitting up. In the past he had suffered from cough in the winter, but his respiratory infections were never severe or prolonged. He had not noticed any ankle œdema.

Examination

He was enormously obese, dyspnœic, and dark blue in the face. His buccal mucosa was also deeply cyanosed, and he was drowsy though not twitching. His dyspnœa prevented him from sustaining a conversation. His temperature was 98·6°F and he was sweating profusely. He had no finger clubbing. His respiration was 36 per minute, almost entirely abdominal. Apart from a few crepitations at the right base, there were no adventitious sounds in the chest. His pulse-rate was 130 per minute and regular: his blood-pressure 160/85 mm. Hg. The heart sounds were distant but normal, there was no peripheral œdema, and the neck-veins were not distended. Examination of his abdomen was unrewarding because of his obesity. His central nervous system showed no abnormalities. Urine: specific gravity 1002; no abnormal constituents.

We made the diagnosis of " cardiorespiratory syndrome of extreme obesity " and admitted him to hospital.

Investigations

The chest X-ray, though difficult to interpret, was normal; and the sputum yielded a normal bacterial flora. The E.C.G. changes were non-specific: isoelectric T-waves in V_5, diphasic T-waves in V_6, and slight depression of the ST segment in V_6 and V_F.

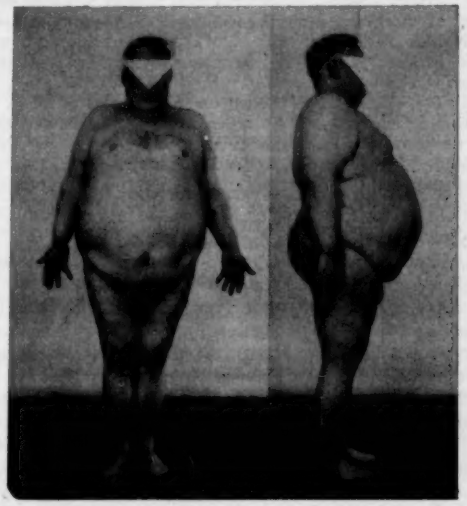
Blood-examination showed: Hb 17·5 g. per 100 ml., red-cell count 6·02 million per c.mm., packed-cell volume 63%, colour-index 0·98, mean corpuscular diameter 7·7μ, mean corpuscular volume 105 cμ, mean corpuscular hæmoglobin concentration 28%, nucleated red cells 6 per 200 white cells, white-cell count 14,000 per c.mm. (74·5% polymorphs, 16·5% lymphocytes, 8·5% monocytes, 0·5% eosinophils). The serum-sodium was 137, the potassium 4·5, the chloride 90, and the bicarbonate 32 mEq. per litre: the serum-pyruvate was 0·8 mg. per 100 ml.

Liver and kidney function were somewhat impaired: the serum-bilirubin was 0·4 mg. per 100 ml., the thymol-turbidity 4 units, the serum-alkaline-phosphatase 7·0 King-Armstrong units, and bromsulphthalein-retention 10·9% after forty-five minutes The serum-albumin was 3 and the serum-globulin 3·6 g. per 100 ml. The blood-urea was 60 mg. per 100, but the patient also had a mild urinary infection.

The circulation-times were prolonged: arm-to-lung was 25 sec. (ether), and arm-to-tongue 26 sec. (saccharine). The arterial oxygen-saturation was measured three weeks after admission: it was 47·5% at rest, the patient breathing room air. His vital capacity was 2·2 litres (37% of normal), and his maximum breathing capacity 40·6 litres per minute (29% of normal). His blood-volume was estimated by the radioactive chromate method a month after admission: the total volume was 8·89, and the plasma-volume 3·83 litres (131% and 70% of the expected values respectively).

Treatment and Progress

We gave the patient continuous oxygen at a rate of three litres a minute through a disposable plastic face-mask (Westlake and Campbell 1958) and kept him on an 800-calorie diet. While he was on oxygen his face became less cyanosed; but, despite intravenous and intramuscular nikethamide, it quickly reverted to its dark blue colour when the mask was taken away. He did, however, derive considerable benefit from intermittent oxygen and



Photograph taken of patient on Feb. 17, when weight was 21 st.

improved gradually. As he was highly cooperative his diet could be progressively reduced to 400 calories and then to 250 calories a day with vitamin supplements that included 100 mg. aneurine hydrochloride. An intramuscular injection of 2 ml. 'Neptal' produced a diuresis of 128 oz. on Feb. 1, but a repeat injection no longer elicited a response of this order.

On admission he had been too heavy to be weighed on the ward scales; but after two weeks on a 250-calorie diet his weight, measured on the scales used in the hospital stores, was 24 st. He was 67 in. high. By Feb. 11 he was 22 st. 10 lb.; and on Feb. 25, when his weight was 21 st., he was no longer cyanosed at rest. He was gradually mobilised and by the beginning of March he was able to walk up and down a flight of stairs and along a ward without becoming short of breath. He then weighed 20 st. 7 lb.

During his hospital stay we found that he had a proteus urinary infection. It responded to a seven-day course of nitrofurantoin ('Furadantin'). He was discharged on a 1000-calorie diet, free of dyspnœa and no longer cyanosed, on March 3.

Discussion

The syndrome of cardiorespiratory failure associated with extreme obesity was first recognised by Kerr and Lagan in 1936. Since then cases have been reported by Auchinloss et al. (1955), Burwell et al. (1956), Counihan (1956), Seide (1957), Weil (1955), Carroll (1956), and Siecker et al. (1955). The essential features of the syndrome are obesity, cyanosis, arterial oxygen desaturation, and polycythæmia; others, such as somnolence, twitching, periodic respiration, and varying degrees of right-sided heart-failure are less constant. In most fatal cases the respiratory system showed no abnormality at postmortem examination (Counihan 1956, Seide 1957); but, even when there is evidence of chronic respiratory disease, this does not exclude extreme obesity as the precipitating cause of failure. That intrinsic pulmonary disease is not by itself serious enough to produce cor pulmonale was shown by Lillington et al. (1957): they included in their series 3 patients with respiratory disease in whom failure was reversed by loss of weight.

The immediate cause of the cardiorespiratory failure is alveolar hypoventilation, and it is possible to explain this by three mechanisms:

1. Extra work is necessary to maintain alveolar ventilation by moving the fat-laden abdomen and thorax. The obese person therefore sets his respiratory centre to work at a subnormal level of energy expenditure, and this leads to alveolar hypoventilation. Lillington et al. (1957) illustrated this in some of their patients by showing that maximal voluntary respiratory effort could restore arterial oxygen saturation to normal.
2. The diaphragm is pushed up by the mass of fat in the abdomen, and respiratory movements are further restricted by the cuirasse effect of the fat on the chest.
3. Mediastinal fat deposits encroach on the lungs.

The 47% arterial oxygen saturation found in our patient is the lowest so far recorded: unfortunately, his oxygen saturation when breathing 100% oxygen was not estimated. In those patients in whom this test was done, oxygen saturation was restored to 100%.

Alveolar hypoventilation is responsible for the development of secondary polycythæmia. This may remit once the patient has lost weight: its treatment by phlebotomy —especially in the early stages when the increased red-cell volume is a physiological response to anoxæmia—is illogical (Seide 1957, Lillington et al. 1957, Auchinloss et al. 1955). Anticoagulant therapy, on the other hand, may be beneficial, since it reduces the risk of thrombosis.

Anoxæmia also causes right ventricular failure, presumably as a result of the pulmonary arterial hypertension which has been demonstrated by cardiac catheterisation (Siecker et al. 1955). It is difficult to explain why the systemic arterial pressure remains normal even though readings tend to be high on fat arms (Smirk 1957).

The liver and the kidneys may also suffer: Weil (1955) suggested that pressure on them by the surrounding fat could account for their impaired function. In our patient the alcoholism and renal-tract infection made it difficult to evaluate the abnormal results of the liver and kidney function tests.

In contrast to the sitting-up position so commonly adopted by people with other types of cor pulmonale, those with this syndrome prefer to be semirecumbent.

The mainstay of their treatment is a low-calorie diet: a regimen of 250 calories a day was well tolerated by our patient and rapidly improved his symptoms. Oxygen can also be given, but the flow-rate should not exceed three litres a minute at first. This will prevent respiratory depression which might be caused by the rapid removal of the anoxæmic stimulus to the respiratory centre (Westlake and Campbell 1958). Other therapeutic measures used in cor pulmonale—mercurial diuretics, low-salt diet, and digitalis—have an important place in the management of the syndrome.

Various names have been given to this condition—heart-failure due to extreme obesity (Seide 1957); cardiopulmonary failure in obesity (Carroll 1956); cardiorespiratory syndrome of obesity (Lillington et al. 1957), cardiopulmonary syndrome associated with extreme obesity (Siecker et al. 1955). In their erudite and amusing article Burwell et al. (1956) called it "extreme obesity associated with alveolar hypoventilation—a Pickwickian syndrome"; Pickwick himself was neither cyanosed nor somnolent, and he was able to run all the way to his house in Dingley Dell after falling through the ice. Joe, the fat boy, clearly had only obesity as his qualification, and the suggestion of the *New England Journal of Medicine* (1957) that the syndrome should be called "Fat Joe's Folly" must therefore be rejected. Scientific accuracy is best served by the purely descriptive title of "cardiorespiratory syndrome of extreme obesity".

Summary

A successfully treated case of cardiorespiratory failure in a man weighing 26 st. is described and previously reported cases are briefly reviewed.

The name "cardiorespiratory syndrome of extreme obesity" seems best for this condition.

Since it can be cured by a low-calorie diet, it needs to be distinguished from other types of cor pulmonale.

I wish to thank Dr. H. T. Howat for much helpful criticism and for permission to publish; the department of cardiology, for measurements of vital capacity, maximal breathing capacity, and arterial oxygen saturation; and Dr. R. Ollerenshaw, of the department of medical illustration, for the photograph. I also wish to thank Dr. C. D. R. Pengelly for his estimation of the blood-volume.

REFERENCES

Auchinloss, J. H., Jr., Cook, E., Renzetti, A. D. (1955) *J. clin. Invest.* **34**, 1537.
Burwell, C. S., Robin, E. D., Whaley, R. D., Bickelmann, A. G. (1956) *Amer. J. Med.* **21**, 811.
Carroll, D. (1956) *ibid.* p. 819.
Counihan, T. B. (1956) *Brit. Heart J.* **18**, 425.
New England Journal of Medicine (1957) **257**, 1238.
Kerr, W. J., Lagen, J. B. (1936) *Ann. intern. Med.* **10**, 569.
Lillington, G. A., Anderson, M. W., Brandenburg, R. O. (1957) *Dis. Chest*, **32**, 1.
Seide, M. J. (1957) *New Engl. J. Med.* **257**, 1227.
Siecker, H. O., Ester, E. H., Jr., Kelser, G. A., McIntosh, H. D. (1955) *J. clin. Invest.* **34**, 916.
Smirk, E. H. (1957) High Arterial Pressure. London.
Weil, M. H. (1955) *J. Amer. med. Ass.* **159**, 1592.
Westlake, E. K., Campbell, E. J. M. (1958) *Brit. med. J.* i, 709.

Preliminary Communications

PLASMA-HYDROCORTISONE LEVELS DURING CORTISONE ADMINISTRATION

THE report of the British committee [1] on the treatment of rheumatoid arthritis with cortisone has renewed interest in the use of steroids or corticotrophin (A.C.T.H.) in this and other diseases. It has been pointed out [2] that oral cortisone may be less effective than corticotrophin, since the steroid given by mouth must first pass through the liver where it may be rapidly metabolised. Few data are available concerning plasma-hydrocortisone levels during cortisone therapy, and we here record some facts which may throw new light on long-term steroid administration.

During a study of the effect of œstrogen on hydrocortisone metabolism, cortisone acetate (100 mg.) was given once daily intramuscularly to four individuals. Before the injection plasma was drawn each day at 8 A.M. for estimation of hydrocortisone by the method of Peterson et al.[3] 24-hour urine collections were made and 17-hydroxycorticosteroids measured as Porter-Silber chromogens after glucuronidase hydrolysis.

The results are shown in the accompanying figure. There seems to be a steady fall in the levels of plasma-hydrocortisone in (1) and (3). In (2) and (4) such a fall is not seen over five- and six-day periods. The recovery of administered steroid in the urine is small, but this has previously been seen when cortisone acetate was given intramuscularly.[4] In all cases there is a tendency for the urinary excretion to rise. These data suggest that there is more rapid metabolism of the steroid and they cannot be explained by variability in absorption from the muscles.

DISCUSSION

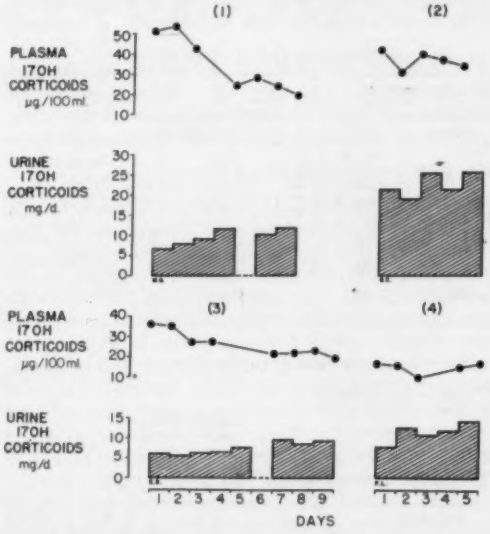
Only further study will show whether altered steroid metabolism commonly accompanies failure to respond to cortisone. The administration of œstrogen reverses this fall in plasma-hydrocortisone during cortisone therapy,[5] and raises the plasma-hydrocortisone in individuals not given cortisone. Similar alteration of hydrocortisone metabolism is produced by adminstration of 17α-ethyl-19-nortestosterone and this has been shown to be due to an increase in the specific hydrocortisone-binding protein.[6] It is possible, therefore, that simultaneous treatment with 17α-ethyl-19-nortestosterone might prevent this fall in plasma-hydrocortisone during continued cortisone therapy. However, the altered metabolism of hydrocortisone which is brought about by œstrogen seems to revert to normal after several months, despite continued œstrogen administration [7]: the same might apply to the effect of 17α-ethyl-19-nortestosterone.

IVOR H. MILLS *
M.D. Cantab., PH.D. Lond., M.R.C.P.

FREDERIC C. BARTTER
M.D. Harvard

Section of Clinical Endocrinology, National Heart Institute, National Institutes of Health, Bethesda, Maryland

1. Report of Joint Medical Research Council and Nuffield Foundation Committee, *Brit. med. J.* 1957, i, 847.
2. Bush, I. E. *ibid.* 1957, ii, 1542.
3. Peterson, R. E., Karrer, A., Guerra, S. L. *Analyt. Chem.* 1957, **29**, 144.
4. Prunty, F. T. G. *Brit. med. J.* 1956, ii, 615, 673.



Estimation of 17-hydroxycorticosteroids in plasma and urine of four individuals receiving 100 mg. of cortisone acetate intramuscularly daily.

ACTION OF INSULIN ON ISOLATED RAT SPINAL CORD

IT is generally accepted that insulin has no effect on the carbohydrate metabolism of the central nervous system.[8 9] This conclusion is based, inter alia, on the negative results in investigations using brain slices incubated in insulin-containing media.[10]

The rat-diaphragm method has been used for many years in studies of carbohydrate metabolism of muscle. Among its advantages are the high surface/weight ratio combined with the preservation of intact cell membranes (a rat hemidiaphragm of 100 mg. has a surface area of about 300 sq. mm.).

Takane,[11] first using the isolated-rat-diaphragm technique, demonstrated the effect of insulin in vitro on the glucose uptake, where investigators working with minced muscle had been unable to demonstrate insulin action in vitro. This difference in results pointed clearly to the importance of preserved cell membranes as a prerequisite for demonstrating the insulin effect. After the revival of the method by Gemmill,[12 13] the method has been widely used in studies concerning the intermediary carbohydrate metabolism and in plasma-insulin assays.

Similar techniques have been described using the rat epididymal fat tissue [14] and the crystalline lens.[15] In both these techniques intact cell membranes are preserved.

In an attempt to reinvestigate the action of insulin (and also of other compounds) on the central nervous system we chose the rat spinal cord as having the advantage of intact cell membranes. An acceptable surface/weight ratio was found. A rat-spinal-cord piece of 100 mg. has a surface area of about 125 sq. mm. (taken from a rat weighing about 100 g.). The exterior cell membranes are preserved with the pia mater, which remains on the specimen (except, of course, in the cut ends of the specimen).

* Medical Research Council (Eli Lilly) travelling fellow.
Present address: Department of Chemical Pathology, St. Thomas's Hospital, London, S.E.1.

5. Mills, I. H. Meeting Abstracts, Endocrine Society, New York, 1957.
6. Chen, P. S., Jr., Mills, I. H., Bartter, F. C. 4th International Congress on Biochemistry, Vienna, 1958.
7. Mills, I. H. M.D. Thesis, University of Cambridge, 1956.
8. McIlwain, H. Biochemistry and the Central Nervous System. London, 1955.
9. Renold, A. E., Ashmore, J., Hastings, A. B. *Vitam. & Horm.* 1956, **14**, 170.
10. Beloff-Chain, A., Catanzaro, R., Chain, E. B., Masi, I., Pocchiari, F. *Proc. roy. Soc.* B. 1955, **144**, 22.
11. Takane, R. *Biochem. Z.* 1926, **171**, 403.
12. Gemmill, C. L. *Bull. Johns Hopk. Hosp.* 1940, **66**, 232.
13. Gemmill, C. L., Hamman, L. *ibid.* 1941, **68**, 50.
14. Martin, D. B., Renold, A. E., Dagenais, Y. M. *Lancet*, 1958, ii, 76.
15. Ross, E. J. *Medicine*, 1956, **35**, 355.

TABLE I—EFFECT OF INSULIN ON GLUCOSE UPTAKE OF SPINAL-CORD TISSUE FROM UNTREATED RATS

Exp. no.	Level of insulin in medium (I.U. per ml.)	Average glucose uptake						P
		−Insulin		+Insulin		Difference between glucose uptakes		
		mg. per g. w.w. per hr.	No. of spinal-cord pieces	mg. per g. w.w. per hr.	No. of spinal-cord pieces	mg. per g. w.w. per hr.	%	
79	10^{-4}	2·0 ± 0·29	8	3·1 ± 0·33	8	+1·1	+54·9	<0·05
80	10^{-3}	2·3 ± 0·11	8	3·9 ± 0·36	8	+1·6	+69·6	<0·01
68	10^{-2}	4·5 ± 0·26	12	6·7 ± 0·44	12	+2·2	+48·8	<0·001
90	10^{-1}	3·2 ± 0·18	6	4·2 ± 0·26	6	+1·0	+31·2	<0·02
—	10^{-1}	4·0 ± 0·30	6	5·2 ± 0·21	6	+1·2	+30·0	<0·01

METHODS

Female albino rats (Wistar strain), weighing 80–140 g. and fasted for 24 hours, were used. Since any mechanical lesion of the central nervous system seemed undesirable in these experiments, the spinal cords were excised from anæsthetised animals. Anæsthesia was produced in the animals by inhalation of a mixture of 50% carbon dioxide and 50% oxygen for 2–3 minutes.

When the rat was anæsthetised it was placed in a prone position and its four extremities were pinned to the corkboard. A midline incision was drawn from the occiput to the sacrum and the skin on the back dissected free of the underlying tissues. Now a block consisting of the lumbar, thoracic, and cervical parts of the vertebral column and a greater part of the attached longitudinal back muscles was isolated by means of a strong pair of scissors. First a cross-section of the vertebral column was made just proximally to the pelvis, and next the lumbar muscular plates and the ribs on both sides were cut as near the vertebral column as possible. The vertebral column was then isolated from the head by a cross-section between the atlas and the skull base. The vertebral column thus isolated was pinned to the corkboard, again in a "prone" position. As much as possible of the longitudinal back muscles was cut off by a pair of scissors. The arches of the vertebræ were cut as near to their origins as possible—i.e., as laterally as possible—starting in the cervical part and continuing caudally. In this part of the procedure a Gillette scalpel was used (handle no. 3, blade E). The scalpel was kept in a vertical plane parallel to the long axis of the vertebral column. After the two origins of a few vertebral arches had been cut, the arches with their intervening ligaments and muscles were removed. For this purpose and for all handling of the spinal cord we used a small, soft arterial clamp (designed by A. Carrel). The rest of the vertebral arches were removed in a similar way. Now the spinal nerve-roots were cut with a pair of iris scissors and the isolated spinal cord was transferred to a filterpaper-covered block of ice. Here the part between the cervical and the lumbar swelling was divided into pieces about 10 mm. long, giving three individual pieces weighing approximately 50–80 mg. each.

The isolated pieces of spinal cord were now soaked in ice-cold medium. The preparation for incubation and the incubation itself was exactly as in rat-diaphragm experiments reported earlier.[16] When all spinal cord pieces were prepared, they were transferred to incubation flasks and aerated at 4°C for 30 seconds with a mixture of 95% oxygen and 5% carbon dioxide. Each piece of spinal cord was incubated separately. After aeration the flasks were placed in an incubation apparatus of the Dubnoff type.[17] Incubation took place at 37° C and lasted for 90 minutes, the rate of oscillations being 84–88 per min. After the incubation the flasks were again placed in an icebath. The pieces of spinal cord were blotted with filterpaper and weighed rapidly. The wet weights (w.w.) so obtained did not differ significantly from wet weights obtained by weighing before the incubation. The incubation medium was a modified Gey and Gey's buffer[18] (NaCl 0·700%, KCl 0·037%, $NaHCO_3$ 0·227%, $CaCl_2$ 0·017%, Na_2HPO_4 0·015%, KH_2PO_4 0·003%) to which was added glucose to a final level of 300 mg. per 100 ml. The incubation flasks, which were closed with a rubber stopper, had a volume of approximately 35 ml., and in all cases 2 ml. of medium was used. Glucose was determined by the method of Nelson and Somogyi.[19]

Glucose uptake was calculated from the decrease of glucose level in the medium during the incubation and expressed as:

16. Rafaelsen, O. J. *Metabolism* (in the press).
17. Dubnoff, J. W. *Arch. Biochem.* 1948, **17**, 327.
18. Gey, G. O., Gey, M. K. *Amer. J. Cancer*, 1936, **27**, 45.
19. Somogyi, M. *J. biol. Chem.* 1952, **195**, 19.

TABLE II—EFFECT OF ALLOXAN ON GLUCOSE UPTAKE IN EXPERIMENTS WITH RAT SPINAL-CORD TISSUE

Exp. no.	Days from all. inj.	Blood-sugar at death (mean and range) (mg. per 100 ml.)	Average glucose uptake						P
			Control animals		Alloxan diabetic animals		Difference between glucose uptakes		
			mg. per g. w.w. per hr.	No. of spinal-cord pieces	mg. per g. w.w. per hr.	No. of spinal-cord pieces	mg. per g. w.w. per hr.	%	
87	18	237 (122–335)	3·2 ± 0·28	7	2·4 ± 0·17	7	−0·8	−25·0	<0·05
99	30	470 (345–624)	2·8 ± 0·17	8	1·8 ± 0·15	8	−1·0	−35·7	<0·001
128	44	392 (271–624)	4·1 ± 0·37	11	3·6 ± 0·25	11	−0·5	−12·2	>0·05
130	50	316 (109–477)	4·7 ± 0·33	11	3·6 ± 0·38	11	−1·1	−23·4	<0·05

TABLE III—EFFECT OF INSULIN ON GLUCOSE UPTAKE OF SPINAL-CORD TISSUE FROM ALLOXAN DIABETIC RATS

Exp. no.	Days from all. inj.	Blood-sugar at death (mean and range) (mg. per 100 ml.)	Level of insulin in medium (I.U. per ml.)	Average glucose uptake						P
				−Insulin		+Insulin		Difference between glucose uptakes		
				mg. per g. w.w. per hr.	No. of spinal-cord pieces	mg. per g. w.w. per hr.	No. of spinal-cord pieces	mg. per g. w.w. per hr.	%	
128	44	392 (271–624)	10^{-4}	3·6 ± 0·25	11	4·9 ± 0·36	11	+1·3	+ 36·2	<0·01
130	50	316 (109–477)	10^{-3}	3·6 ± 0·38	11	4·5 ± 0·29	11	+0·9	+ 25·0	>0·05
99	30	470 (345–624)	10^{-1}	1·8 ± 0·15	8	4·1 ± 0·31	8	+2·3	+127·6	<0·001

mg. glucose per g. spinal cord W.W. per 60 min. In each experiment 12–24 pieces of spinal cord were used, and average values were calculated for control spinal-cord pieces and for drug spinal-cord pieces. "Pairing" of pieces of similar size for incubation in drug-containing flasks and control flasks was aimed at, but it was not sought to pair spinal-cord pieces belonging to the same animal.

Glucagon-free insulin containing 27 international units (I.U.) per mg. was employed in the experiments in concentrations ranging from 10^{-1} to 10^{-4} I.U. per ml. in the incubation medium.

The production of diabetes in the rats by a single intraperitoneal injection of alloxan was exactly as in rat-diaphragm experiments reported elsewhere.[20] The alloxanised rats used in the experiments all had moderate or severe diabetes of 18–50 days' duration.

RESULTS

Table I shows that isolated rat-spinal-cord pieces incubated similarly to isolated rat hemidiaphragms have a definite glucose uptake. The average uptake is of the order of 2·0–4·5 mg. per g. spinal cord W.W. per 60 min. The day-to-day variation is rather large, as has been observed in rat-diaphragm experiments.[16 21] The scatter of the values on the individual experiment days (indirectly given in the accompanying tables as values for standard error of mean) were also of the same order of magnitude as we found in rat-diaphragm experiments.[16]

Table I also shows that the presence of insulin in the incubation medium causes a statistically significant increase of the glucose uptake. The average increase of glucose uptake is about 50% with insulin in the incubation medium ranging from 10^{-1} to 10^{-4} I.U. per ml. In this range no correlation is evident in these preliminary experiments between insulin level and increase of glucose uptake.

Table II shows that spinal-cord pieces isolated from alloxan diabetic rats have a reduced glucose uptake. The average decrease of glucose uptake is about 25%, and the decrease is statistically significant in 3 out of 4 experiments. In rat-diaphragm experiments with hemidiaphragms isolated from the same alloxan diabetic rats that were used in these spinal-cord experiments we obtained a decrease of glucose uptake of comparable magnitude.[20]

Table III shows that the addition of insulin to the incubation medium increases the glucose uptake of spinal-cord pieces from alloxan diabetic rats. The increase of glucose uptake was highly significant in 2 out of 3 experiments.

These results indicate that insulin acts on the glucose uptake of the spinal cord. The spinal cord is a very special part of the central nervous system, and it would be hazardous to conclude that insulin had an effect on the glucose uptake of the brain because an effect on the glucose uptake of the spinal cord has been demonstrated. The spinal cord may have more metabolic features in common with peripheral nerves than with brain. In recent experiments in our laboratory we found a clear-cut effect of insulin on glucose uptake in isolated rat sciatic nerve, whereas incubation experiments with brain slices have so far given inconsistent results. The cell membranes were preserved in the experiments with isolated rat spinal cord and sciatic nerve, but not in the brain-slice experiments, and in experiments with isolated muscle the importance of intact cell membranes is evident.

Further experiments indicate that insulin increases the glucose uptake of brain-cortex slices (having one intact pia-covered surface), whereas following slices (having two artificial surfaces) are uninfluenced by insulin.

20. Rafaelsen, O. J., Lundbæk, K. Unpublished.
21. Vallance-Owen, J., Hurlock, B. *Lancet*, 1954, i, 68.

SUMMARY

A technique of isolating rat spinal cord for incubation experiments is described.

The results of preliminary experiments were:

1. The basal glucose uptake was 2·0–4·5 mg. glucose per g. spinal cord wet weight per 60 min.

2. Insulin in vitro in concentrations from 10^{-1} to 10^{-4} I.U. per ml. increased the glucose uptake by 50%.

3. Spinal-cord tissue from alloxan diabetic rats had a 25% decreased glucose uptake.

4. Insulin increased the glucose uptake of spinal-cord tissue from alloxan diabetic rats.

I am indebted to Miss Nancy Pedersen and Miss Bodil Kjer for their brilliant assistance in the experiments and the analyses. This investigation was supported by a Ford Foundation grant. Glucagon-free insulin was generously supplied by Nordisk Insulin-laboratorium, Gentofte, Denmark.

Clinic of Psychiatry and
II Clinic of Internal Medicine,
Aarhus University School of Medicine,
Denmark

OLE J. RAFAELSEN
M.D. Copenhagen
Research assistant

Medical Societies

HEBERDEN SOCIETY

THE society met at Stoke Mandeville Hospital, Aylesbury, on Oct. 11.

Temporal Arteritis

Dr. M. SAXTY GOOD (Aylesbury) said that in his series of 20 patients with temporal or giant-cell arteritis headache had been a prominent feature in all; tender and thickened temporal arteries in 19; constitutional illness, anorexia, and fever in 16; pain and stiffness of the jaws in 9; painful neck in 9; and pains in the muscles and limbs in 10. 12 had had eye involvement, of whom 3 not treated with cortisone had become suddenly blind. The average duration of disease after biopsy in the patients not receiving steroids and in 8 patients receiving steroids was 5·4 and 2·5 months respectively. His experience and that of others suggested that early biopsy for diagnosis, followed by cortisone treatment, could shorten the disease and prevent blindness.

Pleural Effusion with Rheumatoid Arthritis

Dr. A. R. HORLEY and Dr. MALCOLM THOMPSON (Newcastle-upon-Tyne) had found instances of pleural effusion complicating rheumatoid arthritis in 8 out of 52 men and 1 out of 128 women, as against only 1 out of 180 control patients without rheumatoid arthritis. In 5 men the pleural effusion was an inaugural event in the development of the arthritis.

Tuberculous Lung Nodules in Rheumatoid Arthritis

Dr. C. J. BARFORD (London) reported the case of a woman with rheumatoid arthritis who developed fever and pericarditis and a positive lupus-erythematosus-cell test after five years of steroid therapy. She also had unusual nodules at the lung bases, which at necropsy proved to be tuberculous.

Treatment

Dr. H. F. WEST (Sheffield) opened a discussion on the new steroids triamcinolone and dexamethasone. 28 patients with rheumatoid arthritis treated with prednisolone were allocated at random to continue with the drug or change to triamcinolone, on a roughly "tablet-for-tablet" basis. Those who changed had fared slightly but not significantly better, but the average dose (9 mg.) of triamcinolone was probably on the high side and was liable to produce excessive side-effects. In another group of patients steroid hypertension was not altered by change to triamcinolone. The new drug had been useful to some patients who were excessively wakeful on prednisolone, but the tendency to reduce appetite and cause loss of weight and weakness was a disadvantage.

Other speakers reported that triamcinolone caused excessive loss of muscle tissue in some patients, giving the clinical appearance of a myopathy. Experience of dexamethasone was limited but it seemed an effective drug. Caution was needed, since it had been reported that dexamethasone could suppress the adrenal cortex in subtherapeutic doses—a finding so far not confirmed. Some speakers were concerned because new steroids, each accompanied by claims to be more effective than its predecessors, were being frequently released for general use. Clinical trials to establish or disprove such claims took so long that the drug tested was "obsolete" before it could be reported on. Thus informed assessment of potentially dangerous drugs already in use was becoming more and more difficult.

Dr. J. F. BUCHAN (London) had treated 38 ambulatory patients suffering from rheumatoid arthritis with chloroquine sulphate. In a double-blind trial certain of these patients were changed to dummy tablets after an interval. Objective assessment of disease activity and joint involvement at three and six months showed chloroquine sulphate to be clearly, but weakly, effective in this disease.

Stainable bone-marrow iron had been studied by Dr. A. G. S. HILL and Dr. C. L. GREENBURY (Stoke Mandeville). It proved to be absent or scanty in 56% and excessive in 22% of 120 patients with rheumatoid arthritis, but there was no correlation with circulating hæmoglobin or mean corpuscular hæmoglobin concentration. Excess iron was more often found in active disease; and a group of patients with inactive disease, anæmia, and absent marrow iron could be distinguished. Their anæmia consistently responded to intravenous iron; but this response was not necessarily specific, since several anæmic patients with excess marrow iron had also shown major rises of hæmoglobin; in such cases response was associated with improvement in the disease. Remissions of disease induced by steroids were accompanied by rise of hæmoglobin and disappearance of excess concentration of marrow iron.

Dr. J. J. R. DUTHIE (Edinburgh) had confirmed, in a controlled trial, that in rheumatoid arthritis large doses of intravenous iron (up to 5 g.) had induced remissions of disease. As part of this remission there was an improvement in the accompanying anæmia.

Rheumatoid Agglutinating Factor

Dr. W. R. M. ALEXANDER (Edinburgh) described experiments in purifying the rheumatoid agglutinating factor, based on its adsorption to bentonite particles coated with rabbit gamma-globulin, and subsequent elution by veronal buffer at pH 8·6 and at 56°C. Results were best when the euglobulin fraction of rheumatoid-arthritis serum was used as the starting material. Rheumatoid agglutinating factor purified in this way had been used to immunise rabbits and produce a specific antiserum capable of neutralising the agglutinating activity.

Reviews of Books

Radiation Hazards and Protection

D. E. BARNES, G.M., B.SC., A.M.I.E.E., A.INST.P., superintendent, health physics, A.W.R.E., Aldermaston; DENIS TAYLOR, M.SC., PH.D., M.I.E.E., F.INST.P., late head of electronics division, A.E.R.E., Harwell. London: George Newnes. 1958. Pp. 178. 30*s*.

THE time is ripe for a detailed book on radiation protection, and the authors are to be congratulated on putting so much information in this short book. The contents are not as general as the title implies: discussion is limited to problems associated with radioactivity, and X rays are not considered. The introductory chapters are well-written and up to date, both in content and in concept. It is clear, however, that the authors have never tried measuring in "pastille units". The sections on biological effects and permissible doses are good, but the selection of elements for which permissible doses are given omits two or three which are widely used as tracers in medical work. The statement that "leukæmia arises spontaneously in one person per 20,000" should read "in one person per 20,000 *per annum*". Generally, it is clear that much care has gone into the book, which is a pleasure to read.

The sections on instrumentation are excellent in describing the principles of the different pieces of equipment, but a dearth of references and footnotes is a bar to more detailed study. The sections on shielding, contamination, and waste disposal, while giving useful ideas to the medical worker, are primarily written with atomic-energy establishments in mind. "In preparing any solid waste for disposal, it is usual to enclose it in a concrete shell . . ."; not in most hospitals. Nevertheless, the methods of protection are essentially similar, and many of the ideas discussed could, on the right occasion, be very useful even in a small radioisotope laboratory.

It is hard to decide for whom the book is best suited. Not doctors, since the Poisson probability distribution is dismissed in a three-line footnote containing a frightening equation. Not ordinary physicists, since the problems of a changing genetic equilibrium are disposed of in one short paragraph. It has even been facetiously suggested that the book is aimed at those hospital physicists thinking of taking up princely salaries in Atomic Energy. Nevertheless, it should certainly be read by hospital physicists staying in the N.H.S., and by anyone responsible for protection in radioisotope work, because it is one of the few up-to-date, comprehensive, and authoritative books on this subject.

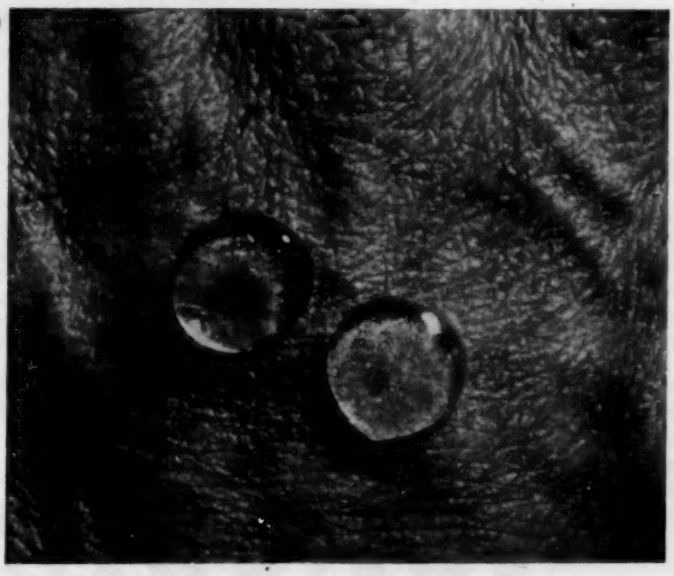
Coccidioidomycosis

MARSHALL J. FIESE, M.D., F.A.C.P., director of health services, Fresno State College, clinical instructor in medicine, Stanford University School of Medicine. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1958. Pp. 253. 72*s*.

No English student is likely to be ploughed if he admits ignorance of coccidioidomycosis. It is a dustborne fungal infection native to certain arid regions in the western hemisphere which attracted more than local attention when it caused a considerable amount of illness among airmen training in those parts. People infected in one of the endemic centres and a few laboratory infections have brought the disease to many of the larger medical centres, and the more omniscient physician now keeps it as a long-shot diagnosis. Because of the rarity of the disease outside the Americas it is a very proper subject for a monograph to be kept on the library shelf, and it would be difficult to write a more inclusive or useful book than this. It is well documented: the pictures are good: it is scholarly and interesting. What is even more important is that it is the work of one who has probably had more personal experience of the disease than any other doctor.

Medical Annual (76th issue. Bristol: John Wright. 1958. Pp. 586. 42*s*.).—When an annual review has passed through 76 editions it is so obvious a success that new issues often receive brief notice. But we must say more than usual about this year's *Medical Annual* because it is arranged in an entirely new way, so that some readers will not recognise their old friend when they open it. Previously it has been arranged alphabetically, a system that lends itself to quick, easy reference—provided that the reader and the maker of the index call diseases by the same name. But inevitably the result is a patchwork: the book cannot be read; it has to be a reference work. Moreover, as the editors, Sir Henry Tidy and Prof. R. Milnes Walker, say, there is a limit to the usefulness of alphabetical arrangement, particularly as names become longer and diseases dissolve progressively into syndromes. So the 1958 edition starts afresh, and the book is now divided into systematic sections. Each stands as a whole and can be read as an entity, and is the usual comprehensive and authoritative summary of the year's work. Not least valuable are the contributors' informal and occasionally pungent comments. The editors have also included four articles on subjects of much topical interest and importance, and these precede the sectional summaries. They are all excellent, particularly that by Dr. P. M. F. Bishop, which gives a lucid exposition of the difficult subject of intersexuality. The changes in the book have been made sensibly and neatly, and this familiar guide is now more attractive and helpful than ever.

WHICH IS WATER?



Try this for yourself. Place a drop of water next to a drop of Predsol* Lotion (Glaxo soluble prednisolone in water). Compare the clarity of the two. Even if you examine the lotion under a microscope you will detect no particles. All the hormone is in solution free to diffuse and exert its maximum therapeutic effect in suppressing inflammation. Spread the lotion on the skin and its other merits are swiftly apparent . . . its smooth, even flow . . . its excellent covering power . . . its complete freedom from undesirable stickiness. Moreover, dosage is flexible, the lotion being issued in two strengths, 0·1% and 0·25%.

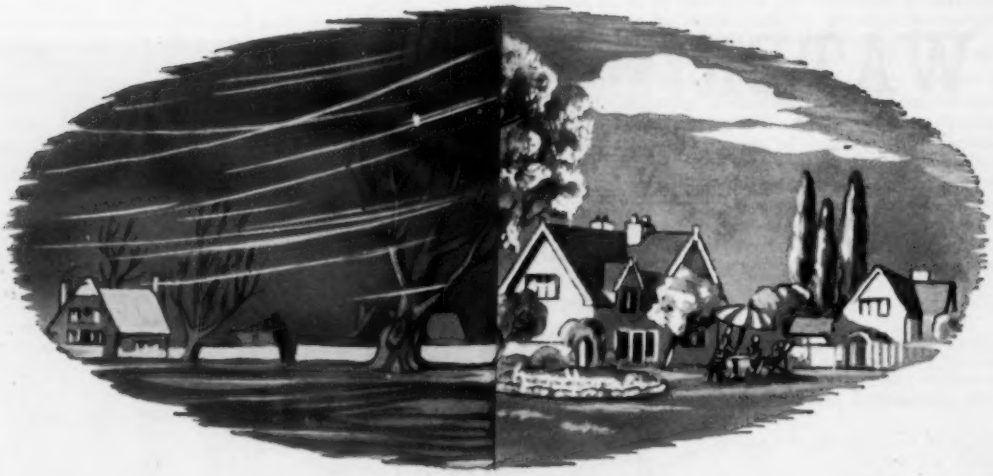
GLAXO LABORATORIES LTD

GREENFORD MIDDLESEX BYRon 3434

Subsidiary Companies or Agents in most countries.

*TRADE MARK

ALL THE YEAR ROUND



COSCOPIN

TRADE MARK

FOR MORE EFFECTIVE CONTROL OF COUGH

Recent publications show that **COSCOPIN**—noscapine (formerly known as narcotine)—**IS CLINICALLY MORE EFFECTIVE THAN CODEINE IN THE SUPPRESSION OF COUGH***

Amer. J. med. Sci. (*1957*), **234**, *191*.
Dis. Chest* (*1957*), **32, *305*.

PRESENTATION:

COSCOPIN LINCTUS
Bottles of 4 fl. ozs. (114 ml.) and 2 litres.

COSCOPIN LOZENGES
Catch-cover of 20 lozenges.

EVANS MEDICAL

EVANS MEDICAL SUPPLIES LTD
LIVERPOOL AND LONDON

672

THE LANCET
LONDON 1 NOVEMBER 1958

Hyaline Membrane

IN the premature infant signs of atelectasis are liable to develop soon after birth. At postmortem examination the changes are characteristic. The lungs are dull red and of the consistence of liver; they are congested and œdematous and show little evidence of aeration; microscopically the alveolar ducts are over-distended and the alveoli collapsed—the appearance of "resorption atelectasis".[1] In about 50% of cases[2] many alveolar ducts and some atria and alveoli are lined by an eosinophilic layer of structureless, homogeneous material, the so-called hyaline membrane. This "membrane" was first described by HOCCHEIM[3] at the beginning of this century; and for many years the condition was regarded as a peculiar form of pneumonia,[4] particularly since affected infants almost invariably died from a pulmonary infection if they survived more than 36 hours after delivery. With the advent of chemotherapy and antibiotics postnatal pneumonia has become less common, and atelectasis with hyaline-membrane formation is a more prominent feature of neonatal pathology. Some workers[5,6] suggest that the alveolar collapse is the important feature of this condition, and that the "membrane", while spectacular, is of secondary importance. Others believe that the membrane, especially when thick and widespread, may close the openings of the atria and alveoli and so hasten the collapse of the lung.

The condition is particularly liable to affect the premature infant. But if the infant has been delivered by cæsarean section or if the mother is a diabetic, babies with a birth-weight of over 2500 g. are liable to a similar affection.[7] Other maternal features, such as age, parity, and race, do not seem to be incriminated. Among premature infants the largest number of cases is found in those weighing 1000–1500 g. at birth[8]; but if the incidence of hyaline membrane is expressed as a percentage of premature infants at risk, the incidence is seen to rise as the birth-weight falls[9]—a finding endorsed by Dr. AVERY and Dr. DROLETTE in their letter this week. It is now largely accepted that a pulmonary hyaline membrane is a feature of neonatal death and is not seen in the stillborn fœtus.[10–12] FARBER[13] first pointed out that the material is present in the air-spaces, chiefly alveolar ducts, of the affected lung and is then spread out in the form of a membrane around the wall of the duct when air is breathed in. When no air enters the lung, as in a stillbirth, a membrane cannot be formed. The membrane has been observed in the lung of an infant who died only 55 minutes after birth, but usually it is scanty and poorly formed if the infant has died in the first 6 hours. The majority of affected infants die within the first 24 hours, but a few survive for 2 or 3 days. One infant with the nephrotic syndrome who died aged 72 days had typical hyaline membrane in his lungs.[14]

The nature of the material from which the membrane is formed and the mode of formation are still uncertain. There is considerable argument as to whether the material forming the membrane is derived from the contents of the amniotic sac or whether it is largely composed of protein which has escaped from the pulmonary circulation into the air-spaces of the lung. For very many years aspiration of amniotic fluid[12,15] or vernix caseosa[13] was thought to be the major factor in the development of a hyaline membrane. Latterly, doubt has been cast on this explanation, and attention has been directed instead to a fundamental disorder of the pulmonary circulation.[16,17] There are several reasons for this change. Firstly, a similar hyaline membrane with almost exactly the same staining characteristics has been reported in adults and older children with various conditions such as epidemic influenza, phosgene poisoning, and acute rheumatism.[7,13] Secondly, amniotic fluid aspirated from the lungs of affected infants is often very scanty, and only in a minority of cases could this apparently have any possible bearing on the development of a membrane. Thirdly, the lungs of an affected newborn infant are intensely congested and œdematous; in not a few cases pulmonary œdema is the most striking pathological finding, and areas of hæmorrhage may also be present. This triad of congestion and œdema, hæmorrhage, and atelectasis with hyaline-membrane formation has been given the name of "pulmonary syndrome of the newborn".[18] The combination of œdema, patchy intra-alveolar hæmorrhage, and membrane formation is taken to indicate severe damage to the capillaries of the pulmonary vascular bed.

Histochemical studies have been carried out in order to determine the nature of the substance lining the alveolar ducts.[7,16,17,19,20] The membrane is strongly eosinophilic and gives a positive reaction with the periodic-acid Schiff technique. It contains no iron, and fat may be present or absent; it was the presence of fat that gave rise to the original supposition that the membrane was vernix caseosa.[13] The ordinary chemical staining techniques for fibrin give a negative result. GITLIN and CRAIG[17] have applied an immunohistochemical technique using fluorescin-labelled antibodies to blood-proteins. They claim that a large part of the hyaline membrane is composed of fibrin. Studies on the

1. Potter, E. L. Pathology of the Fetus and Newborn. Chicago, 1952.
2. Claireaux, A. E. *Postgrad. med. J.* 1954, **30**, 338.
3. Hoccheim, K. Medicinabrat, Dr. Johannes Orth zur Feier seines 25-jährigen Professoren Jubiläums Gewidmet. Berlin, 1903.
4. Johnson, W. C., Meyer, J. R. *Amer. J. Obstet. Gynec.* 1925, **9**, 151.
5. Gruenwald, P. Report of Fifth M. & R. Pediatric Research Conference, 1953.
6. Ranstrom, S. *Acta pædiat., Uppsala*, 1953, **42**, 323.
7. Tran-Dinh-De, Anderson, G. W. *Obstet. Gynec. Survey*, 1953, **8**, 1.
8. Claireaux, A. E. *in* Modern Trends in Pediatrics (edited by A. Holzel and J. P. M. Tizard); p. 52. London, 1958.
9. Silverman, W. A., Silverman, R. H. *Lancet*, Sept. 13, 1958, p. 588.
10. Miller, H. C., Hamilton, T. R. *Pediatrics*, 1949, **3**, 735.
11. Snyder, F. F. *Obstet. Gynec.* 1958, **11**, 599.
12. Blystad, W., Landing, B. H., Smith, C. A. *Pediatrics*, 1951, **8**, 5.
13. Farber, S., Wilson, J. L. *Arch. Path.* 1932, **14**, 437.
14. Kunstadter, R. H., Rosenblum, L. *Amer. J. Dis. Child.* 1954, **88**, 611.
15. Claireaux, A. E. *Lancet*, 1953, ii, 749.
16. Duran-Jorda, F., Holzel, A., Patterson, W. H. *Arch. Dis. Childh.* 1956, **31**, 113.
17. Gitlin, D., Craig, J. M. *Pediatrics*, 1956, **17**, 64.
18. Bound, J. P., Butler, N. R., Spector, W. G. *Brit. med. J.* 1956, ii, 1191.
19. Lelong, M., Laumonier, R., Le Tan Vinh. *Etud. néo-natal*, 1953, **2**, 3.
20. Lynch, M. J. G., Mellor, L. D. *J. Pediat.* 1955, **47**, 275.

neonatal lung with the electron microscope also point to fibrin as a major component of the membrane,[21] despite the fact that the ordinary stains for fibrin give consistently negative results.

Many experimental techniques have been used in an attempt to reproduce a hyaline membrane. These include intratracheal injection of amniotic fluid [4 12 15] or meconium,[2] oxygen poisoning,[21 22 25] bilateral vagotomy,[26 27] X-ray irradiation,[23] carbon-dioxide poisoning,[24] and the administration of analgesics to pregnant rabbits before labour.[11] The experimental approach has thus been in two main directions: firstly, an attempt to show the role of aspiration of amniotic-sac content, and secondly the production of membranes following damage to the lung or pulmonary circulation. Unfortunately none of these experiments are absolutely conclusive, and some are not applicable to the development of the disorder in the newborn human infant. Intratracheal injection of amniotic fluid or debris does not result in the production of generalised membrane in the animal lung, and lesions tend to be scattered. The lesion produced in the lungs of rabbit fœtuses after administration of analgesics to the pregnant doe [11] are more similar to those in the human infant. They are also associated with evidence of heavy aspiration of amniotic-sac content. The easiest way to produce distinct hyaline membrane with severe œdema in the animal lung is by oxygen poisoning.[22] This has led to some speculation as to whether the administration of oxygen to the newborn infant may damage the lungs similarly to the effect of oxygen in the production of retrolental fibroplasia.[25] But an atmosphere of 90–100% oxygen for at least 60–70 hours is required for the production of membrane in the animal lung; most clinicians are aware of the hazard of high oxygen tensions in incubators, and it is unlikely that any infant would be exposed to 100% oxygen for very long.

At present it does not seem possible to decide which hypothesis—that of aspiration of amniotic-sac content or that of damage to the pulmonary capillaries—is the correct one. Indeed some workers [28] have suggested that the aspiration of amniotic-sac content may potentiate the clotting of plasma-protein which has escaped from the pulmonary vessels into the alveoli. It is also possible that the apparent increase of hyaline-membrane formation among infants delivered by cæsarean section may be in some way associated with an increased risk of amniotic-fluid aspiration. Nevertheless the almost invariable association of hyaline-membrane formation with pulmonary œdema, severe pulmonary congestion, and intra-alveolar hæmorrhage seems to suggest that the primary disorder is in the pulmonary circulation. The fact that the majority of affected infants have a birth-weight of under 2500 g. seems to indicate that the membrane is an expression of disordered physiology rather than a pathological lesion in the usual sense. Apparently these small infants find the sudden change from an intra-uterine environment too much for their pulmonary circulation, and plasma-proteins or even red blood-cells are extravasated from the pulmonary vessels into the surrounding air-spaces; the hyaline material is then pressed out into a membrane round the walls of the alveolar ducts by the action of air drawn down into the lungs. The condition is to some extent reversible, since some affected infants recover. But if the œdema and membrane formation are associated with severe atelectasis the outlook is grave; respiratory embarrassment becomes more and more pronounced and the infant dies, often as the result of a terminal massive intraventricular hæmorrhage.

If this view of the development of the membrane should prove to be correct, attempts to "dissolve" the membrane by the use of proteolytic aerosols and other such techniques are doomed to failure. We need to learn more about the state of the pulmonary circulation in the newborn and the response of the pulmonary vessels to the stress of extra-uterine existence.

21. Van Breemen, V. L., Neuztein, H. B., Bruns, P. D. *Amer. J. Path.* 1957, **33**, 769.
22. Bruns, P. D., Shields, L. V. *Amer. J. Obstet. Gynec.* 1951, **61**, 953.
23. Warren, S., Gates, O. *Arch. Path.* 1940, **30**, 440.
24. Meesen, H. *Schweiz. med. Wschr.* 1947, **77**, 1135.
25. Ingalls, T. H. *New Engl. J. Med.* 1954, **251**, 1017.
26. Miller, H. C., Behrle, F. C., Gibson, D. M. *Pediatrics*, 1951, **7**, 611.
27. Farber, S. *J. exp. Med.* 1937, **66**, 405.
28. Laufe, L. E., Stevenson, S. S. *Obstet. Gynec.* 1956 **8**, 451.

Self-medication in Tuberculosis

SOME patients take medicines regularly but others do not. The medicine cupboard full of half-used bottles and boxes is almost a music-hall jest; it has seldom been a subject for serious medical study. But in some diseases self-medication is important. Oral drugs had been used in treating tuberculosis for several years before any serious thought was given to whether the patients were, in fact, taking their medicine when left to themselves. It was, it seems, unthinkingly assumed that prescribing *p*-aminosalicylic acid (P.A.S.) and isoniazid was the same as treating patients with these drugs. Fox [1] points out that there are good reasons to question the dependability of patients with other diseases—for example, diabetes,[2] acute pharyngitis,[3] rheumatic fever,[4] and leprosy. SIMPSON [5] in Edinburgh first drew attention to the high proportion of tuberculous patients treated out of hospital who (as was shown by urine tests for P.A.S.) had not taken their prescribed dose; in his series 24% had negative tests. DIXON et al.[6] in London recorded 50% negative; and WYNN-WILLIAMS and ARRIS [7] at Bedford 49%. Similar studies have now been made in Madras during the extensive investigations on the chemotherapy of tuberculosis conducted by the Indian Council of Medical Research, the Madras Government, the World Health Organisation, and the British Medical Research Council.[1]

Patients are being treated in their homes with cachets containing P.A.S. and isoniazid, attending a clinic weekly for fresh supplies. They are also regularly visited in their homes, and close attention is paid to explaining in

1. Fox, W. *Tubercle, Lond.* 1958, **39**, 269.
2. Joslin, E. P. Root, F. H., White, P., Marble, A., Bailey, C. C. The Treatment of Diabetes Mellitus; p. 431. London, 1947.
3. Mohler, D. N., Wallin, D. G., Dreyfus, E. G. *New Engl. J. Med.* 1955, **252**, 1116.
4. Expert Committee on Rheumatic Diseases. *Tech. Rep. Wld Hlth Org.* 1957, 126.
5. Simpson, J. McD. *Tubercle, Lond.* 1956, **37**, 333.
6. Dixon, W. M., Stradling, P., Wootton, I. D. P. *Lancet*, 1957, ii, 871.
7. Wynn-Williams, N., Arris, M. *Tubercle, Lond.* 1958, **39**, 138.

simple terms the need for long-continued and regular taking of cachets. Urine specimens are collected during frequent but unexpected visits, and these are tested for the presence of P.A.S. Of 58 patients observed for twelve months, 20% during the first six months of treatment, and 14% during the second six months, gave at least one negative result each month. These proportions cannot, of course, be directly compared with those in other series with different methods and frequencies of testing; but they appear not to be grossly different. Certainly, with this intensive, individual home treatment of patients in Madras—far more thorough than is generally adopted in this country—self-medication seems as regular as it is among the better educated patients of Edinburgh, London, and Bedford.

DIXON et al. and WYNN-WILLIAMS and ARRIS found that young women were the least regular takers of the drugs. In hospital, similar studies have shown little irregularity in either sex. The trouble begins when the onus of regular medication falls entirely on the patient in his own home and during his normal daily routine. Previous "education" in hospital seems to have no effect, and those who have begun treatment in hospital are found to be as irregular as those who have not.[8] It has sometimes been uncritically assumed that patients do not take their drugs because of the taste of P.A.S. or the unpleasant gastrointestinal symptoms that it can produce. Certainly, those who suffer from these side-effects take the drug less regularly than those who do not.[7] But the proportion of negative urine tests may still be high even when the patients admit to no ill effects; and it is improbable that failure to take the medicine regularly is greatly influenced by the minor unpleasantness of the P.A.S. in it. Now that a satisfactory simple test for isoniazid in the urine has been devised,[9] it will be possible to carry out similar studies among patients in areas where this drug is regularly used alone.

FOX investigated the reasons for irregularity by close but sympathetic questioning of the patients. Only a very few had minor side-effects; some attributed unassociated minor complaints to the medicine and gave this as their reason for stopping; others did not take the cachets on religious fast days, or because they regarded certain days as inauspicious for medicine-taking. In some patients the improvement of appetite from the treatment brought pangs of hunger that they were unable to satisfy—a tragic indication of the inability of the economic structure to keep pace with medical advance. A large proportion gave no explanation; they forgot or were indifferent. Similar questioning in other societies would certainly bring out different reasons; but forgetfulness and indifference are without doubt the commonest and most important factors in all societies. As FOX says: "In essence, in order to make a patient take medicine regularly morning and night for a year it is necessary to establish a new pattern of behaviour." The next stage should clearly be to study how such a pattern can be most effectively and simply established in a particular environment. Are large pills better than small, pink than white, tasteless than sweet? Is once a day better remembered than twice? On the evidence there seems to be no justification for giving P.A.S. and isoniazid more than twice a day, and if cachets have to be taken to work for the midday dose they will probably be often forgotten. Is it easier to get into the habit of taking medicine in the morning or in the evening? How best can the habit be taught and maintained?

It might reasonably be asked whether entirely regular medication in tuberculosis is necessary, provided the medicine is given in such a form that one drug cannot be taken without the other. Despite the apparently alarming incidence of missed doses many patients recover and remain well. In one study of treatment out of hospital,[10] 6 of 7 patients who relapsed admitted to irregular medicine-taking; but it was not stated what proportion of those who did not relapse also admitted to this. Further investigations of the minimum frequency of self-administration of the anti-tuberculosis drugs that will be effective in different types of disease should be attempted. But such studies would not be easy and their results might not be convincing. Meanwhile it seems that the present dosage schemes must remain, with the exhortations of physicians and health visitors to swallow the medicine night and morning. In tuberculosis rest is giving way to self-medication; treatment thus depends largely on the patients, but physicians cannot yet be satisfied that they know enough to make reasonably sure that their patients help themselves.

8. Rigby, J. P. V. *ibid.* p. 336.
9. Gangadharam, P. R. J., Mitchison, D. A., Subbaiah, T. V., Short, E. I. *ibid.* p. 191.

Annotations

A CORONARY PARADOX

RESEARCH into the ætiology of coronary thrombosis has become so much a matter of biochemistry, dietetics, and demographic epidemiology that it is refreshing to find an unexpected and conceivably most significant observation emerging from straightforward histological studies. The survey of the incidence of mast cells in the coronary arteries carried out by Pomerance[11] at the Royal Free Hospital was based on simple enough reasoning. Mast cells secrete heparin; mast cells are present in the adventitia of the arteries; heparin inhibits thrombosis; so possibly a deficiency of mast cells promotes arterial thrombosis, in which case it might be possible to demonstrate a decrease in mast cells in thrombotic arteries. McGovern[12] stripped the adventitia of veins (which also contain mast cells in that layer) and produced thrombosis in the veins: might not some more physiological version of the same mechanism be at work in the coronary arteries? The idea that an increase in blood coagulability promoted by deficiency of heparin is a major factor in the pathological thrombotic tendency of atheromatous subjects is almost commonplace today, however many difficulties may appear in detail[13]; but it is normally taken as applying to heparin circulating in the blood, not in the vessel wall itself.

In the event Pomerance's results were the precise reverse of those expected. Thrombosis was associated,

10. Tuberculosis Society of Scotland. *ibid.* p. 129.
11. Pomerance, A. *J. Path. Bact.* 1958, **76**, 55.
12. McGovern, V. J. *ibid*, 1955, **69**, 283.
13. Watson, W. C. *Lancet*, 1957, ii, 366.

not with a deficiency of mast cells, but with a constant and considerable excess. The highest counts were found over those segments of arteries which were the actual sites of fresh thrombi. Some local increase, though less notable, was found over areas of atheroma without thrombosis. In addition to the local effect, there is a slighter and less well-proved general effect in the form of a higher mast-cell count in the coronary arteries as a whole in patients with diseases (diabetes, for instance) in which there is a tendency to thrombosis. The increase of mast cells is not a reaction to the presence of thrombus, for it was not seen when the thrombus was not of local origin (embolus or propagated), and it vanished as soon as the thrombus canalised.

There is some Finnish work which affords a partial anticipation of these findings. Sundberg [14] mentions (his details are meagre) finding similar unexpected high mast-cell counts in veins in the presence of thrombosis, and he cites Hjellberg as having the same experience with arteries. Both workers explain the mast-cell increase as a reaction to the thrombus—a view discounted apparently by Pomerance's more detailed investigations.

The hypothesis is thus in any case stood on its head: excess of mast cells seems to be *causing* thrombosis. But Pomerance very properly points out that what may really be happening is an inhibition of secretion of heparin by mast cells; by decreasing the number of empty, unrecognisable mast cells this will raise the apparent count. She suggests further that this may be due to anoxia, so neatly accounting for thrombosis occurring in times both of diminished blood-flow and of exercise. Difficulties with this view are not hard to find; but the precise hypothesis invoked to explain the findings is perhaps not very important at present. This paradoxical finding clearly deserves confirmation in detail; and if it is so confirmed (and there is no reason to suppose it will not be) we shall have to think again about our views on the process of coronary thrombosis and the role in it of changes in the vessel wall itself.

WILSON'S DISEASE

Wilson's disease (hepatolenticular degeneration), which is now known to be associated with abnormalities in the metabolism of copper, is a heredofamilial disorder, Bearn [15] concluded that it is inherited in "an autosomal recessive manner". A survey by Neale and Fischer-Williams [16] is therefore a logical step towards elucidating its pathogenesis. They measured serum-copper levels and urinary excretion of copper in 48 relatives of patients with the disease. Of these 48 relatives, who had no clinical manifestations of the disease, 11 were found to have a significant reduction in the level of serum-copper, and in 5 of the 11 the values were between 47 and 70 μg. per 100 ml. Since the lowest level found in a normal subject was 70 μg., Neale and Fischer-Williams regard these levels as undoubtedly abnormal. They did not find excessive urinary excretion of copper in any of the relatives examined. Clearly there may exist *formes frustes* of the condition in which the only detectable abnormality is a low plasma-copper level.

It would be very interesting to see a similar survey of families of patients with the disease that included estimations of cæruloplasmin levels. As far as is known, it is not the low serum-copper level in itself that is important but the fact that such copper as is present is largely in an abnormal and easily detachable form. It is believed that this may lead to the excessive urinary excretion as well as the abnormal deposition in the tissues.[17] Failure to demonstrate high levels of copper excretion in those relatives with low serum levels might be taken to mean that most of the copper present in the plasma (although smaller in amount) was normally bound. In another paper referring to the same families Bickel et al.[18] describe preliminary investigations by immunological methods in some of these subjects with low serum-copper levels, who were found to have pronounced deficiency of cæruloplasmin. If this finding is fully established it may mean that there is a further factor, as yet unknown, which in some subjects with low serum-copper and cæruloplasmin levels leads to the development of the disease. Meanwhile patients with the disease are distinguishable from their relatives by the excessive amount of copper in the urine.

Bickel et al. also describe the results of attempts to treat the condition. Administration of dimercaprol (BAL) and of calcium edetate ('Versene') led in no case to significant clinical improvement, despite a satisfactory increase in copper excretion. They conclude that no final decision can yet be made as to the value of copper-removing therapy. But they do find that calcium edetate is preferable to dimercaprol as a means of promoting copper excretion, since it may be given more frequently and its effect is more sustained. They do not discuss the possible reasons for the apparent difference between their observations and those of, for example, Denny-Brown and Porter,[19] who reported quite clear improvement following treatment with dimercaprol. This discrepancy may be due to difference in the type of case treated, and it would be wrong to conclude that depletion of copper can never alleviate symptoms. The cases described by Denny-Brown and Porter were all in adults who had "the more chronic pseudosclerotic type of hepatolenticular degeneration". In these cases "the age of onset varied from nineteen to thirty-five years and the illness had run a course of from four to thirteen years before causing the patients to require assistance in eating, dressing, toilet and walking". Bickel et al. treated 9 patients, and of these 6 have died. In these 6 the disease led to death three to six years after the earliest symptom appeared. Further, the age of onset in these cases (which ran a rapid course) was much younger than that in Denny-Brown's and Porter's cases (7–15 years, compared with 19–35). Denny-Brown and Porter indeed suggested that less improvement might be expected in younger patients with the more rapidly progressive form of the disease, basing this suggestion on the greater frequency of cavitating cerebral lesions in the younger patients. If the disease is due to copper intoxication resulting from excessive copper retention dating from birth, patients whose symptoms develop early in life are probably those in whom copper deposition is proceeding most rapidly; accordingly treatment directed at depleting the copper laid down would have to be all the more vigorous to be effective.

Bickel et al. also consider the possibility that purified cæruloplasmin given intravenously may have a place in the treatment of the disease; but they are, as yet, unable to draw any conclusions. If the low level of cæruloplas-

14. Sundberg, M. *Acta. path. microbiol. scand.* 1955, suppl. 107.
15. Bearn, A. G. *Amer. J. Med.* 1953, **15**, 442.
16. Neale, F. C., Fischer-Williams, M. *J. clin. Path.* 1958, **11**, 441.
17. *Lancet*, 1957, i, 976.
18. Bickel, H., Neale, F. C., Hall, G. *Quart. J. Med.* 1957, **26**, 527.
19. Denny-Brown, D., Porter, H. *New Engl. J. Med.* 1951, **245**, 917.

min simply reflects some underlying defect which also leads to accumulation of copper in the body tissues, it is difficult to see what might be gained by raising the level of cæruloplasmin artificially; but this certainly should be tried.

NEONATAL MYOCARDITIS

WHILE investigating an outbreak of poliomyelitis in the village of Coxsackie, Dalldorf and Sickles [1] isolated a hitherto unrecognised filterable agent from the fæces of two children with lower limb paralysis. Attempts to isolate the virus in rhesus monkeys were unsuccessful, but paralysis was induced in newborn suckling mice. This discovery heralded the advent of a new family of viruses, which are now recognised as responsible for such infections as Bornholm disease and herpangina, and also for some epidemics of aseptic meningitis and of neonatal myocarditis. During an epidemic of *Summer-grippe* in adults in Amsterdam in 1955 [2 3] four fatal cases of myocarditis were observed in newborns. The diagnosis was suggested by a preceding febrile illness in three mothers, followed by the onset in their infants of dyspnœa, cyanosis, or pallor; in two instances there were electrocardiographic abnormalities. Necropsy revealed diffuse interstitial myocarditis, and in all instances Coxsackie virus group B, type 4, was isolated from the heart-muscle.

The strain of virus involving the myocardium was similar to non-myocardial strains obtained at the same time from patients with pleurodynia and aseptic meningitis. Whereas the virus produced fever and transient viræmia in two six-month-old monkeys, it caused fatal myocarditis in a two-day-old monkey.

Reports from other countries have also implicated the Coxsackie virus as the cause of neonatal myocarditis—none more convincingly than those from South Africa, which has had maternity-home epidemics in Johannesburg in 1952,[4] in nearby Southern Rhodesia in 1954,[5] and in Cape Town in 1957.[6–9]

The onset of illness in the Cape Town maternity-home epidemic in April and June, 1957, was marked by fever, cyanosis, red throat, limpness, vomiting, and dyspnœa in European infants aged 5–8 days. Disproportionate tachycardia, triple rhythm, and a widespread precordial systolic murmur denoted severe infection, while hepatomegaly due to cardiac failure was of grave prognostic import. Changes consistent with myocarditis were seen in electrocardiographs of each of five infants in whom this examination was made; and the tracings subsequently returned to normal in the four survivors. A group-B, type-3 Coxsackie virus was isolated from the fæces of four who recovered and from the heart of four who died. There appeared to be a clear relation between the duration of illness, the acuteness of the myocardial lesion, and the concentration of virus in the heart-muscle. In an infant who died after 2 days' illness there was acute myocarditis and the myocardial virus titre was very high. At the other extreme, the heart of an infant who died after 11 days' illness showed evidence of tissue repair and the myocardial virus titre was low.

This epidemic occurred at a time when Coxsackie-virus infections were prevalent in the general community, and the probable source of infection was two pregnant women who were admitted with Bornholm disease in the incubation period. The idea that the very young infant is especially susceptible to Coxsackie-virus myocarditis is supported by the observation that only those infants born after the first case in each outbreak became ill or infected, whereas all those born before that date showed no disease and no virus was isolated from their fæces, although all were nursed under the same conditions in a common nursery. The possibility of intra-uterine infection was excluded by the absence of virus excretion or of antibody production in relevant mothers. The vulnerability of the neonate, which is in keeping with that of newborn suckling mice and of monkeys, may be related to the high level of circulating corticosteroids in the newborn; it has been shown that Coxsackie B_3 virus causes myocardial necrosis in adult mice only if they are treated with cortisone.[10]

The Cape Town report underlines the value of teamwork by clinicians, pathologists, virologists, and epidemiologists in tackling an epidemic of an ill-understood infection. Alertness at the onset and full use of modern techniques in identifying the causal agent converted another "idiopathic virus *x* mystery" into an identified infection from which valuable experience has been gleaned. The Cape Town workers stress that Coxsackie-virus myocarditis may be overlooked in a case of sudden death or in the absence of specific investigations. Clearly it is important to study carefully all unexpected deaths in infancy.[11] The frequency of sporadic Coxsackie-virus infection is unknown; but Hosier and Newton [12] draw attention to two fatal cases observed in Ohio in the absence of a community or hospital epidemic, and they suggest that Coxsackie myocarditis can occur in the older child and adult.

RATE OF INFUSION

THERE is much variation in the rate of administration by intravenous infusion of solutions intended to maintain the body content of water and electrolytes. Neyzi et al.[13] have investigated the effects of variation in the rate of administering a multiple-electrolyte solution containing sodium, potassium, chloride, phosphate, and lactate.[14] In preliminary experiments they established that healthy persons responded similarly to intravenous and to oral administration of this solution. They employed three different rates of oral administration, and their volunteers starved for 12 hours before and throughout the 72-hour period of study. In one pair of subjects the 24 hours' ration of solution was given in equal doses at hourly intervals; in another pair the whole 24-hour ration was spread evenly over the first 12 hours of the 24-hour period; and in the third pair the total ration was given during the first 6 hours, which was followed by 18 hours of thirst and starvation.

There were few symptoms in the subjects who received fluid throughout the 24 hours, but in the other two groups thirst and hunger were appreciable during the fasting periods. The steady provision of fluid did not tax in any way the capacity of the body to excrete the added water and electrolyte, but when the fluid was administered during the shorter periods there was wider fluctuation in

1. Dalldorf, G., Sickles, G. M. *Science*, 1948, **108**, 61.
2. Van Creveld, S., De Jager, H. *Ann. pædiat., Basle*, 1956, **187**, 100.
3. Verlinde, J. D., van Tongeren, H. A. E., Kret, A. *ibid.* p. 113.
4. Javett, S. N., Heymann, S., Mundel, B., Pepler, W. J., Lurie, H. I., Gear, J. H. S., Measroch, V., Kirsch, Z. *J. Pediat.* 1956, **48**, 1.
5. Montgomery, J., Gear, J., Prinsloo, F. R., Kahn, M., Kirsh, Z. G. *S. Afr. med. J.* 1955, **29**, 608.
6. Suckling, P. V., Vogelpoel, L. *Med. Proc.* 1958, **4**, 372.
7. Simenhoff, M. L., Uys, C. J. *ibid.* p. 389.
8. Naudé, W. du T., Seltzer, G., Kipps, A. *ibid.* p. 397.
9. Kipps, A., Naudé, W. du T., Don, P., Cooper, E. D. *ibid.* p. 401.
10. Kilbourne, E. D., Wilson, C. B., Perrier, D. *J. clin. Invest.* 1956, **36**, 363.
11. See *Lancet*, Sept. 6, 1958, p. 513.
12. Hosier, D. M., Newton, W. A., Jr. *Amer. J. Dis. Child.* 1958, **96**, 251.
13. Neyzi, O., Bailey, M., Talbot, N. B. *New Engl. J. Med.* 1958, **258**, 1239.
14. Talbot, N. B., Kerrigan, G. A., Crawford, J. D., Cochran, W., Terry, M. *ibid.* 1955, **252**, 856, 898.

the rates of excretion. The 6-hour subjects showed, during the first 3 hours of the period of administration, distinct retention, which was followed by the loss of rather more sodium, potassium, chloride, and water than had been retained; the final losses were larger on the 6-hour and 12-hour regimes than when fluid was taken evenly throughout.

Neyzi et al. indicate clearly that, if the pre-infusion rates of urinary excretion persisted during the rapid administration inflicted on the 12-hour and 6-hour subjects, their body content of water and potassium could have been increased by 1–3·5% and 3–5% respectively; and they remind us that the body content of water or potassium cannot be abruptly increased by much more than 5% without causing intoxication. It is also clear that the rapid loading of the body in this fashion is uneconomical, because of the ultimate larger urinary losses by compensatory diuresis.

The dangers, as well as the relative uselessness, of the rapid administration of a 24-hour ration over only 6 hours during the oliguric period after operations are obvious—particularly where the solution contains potassium or where the patient is an infant, with its less elastic renal excretory capacity. If intravenous maintenance infusions must be administered, they are safest when spread evenly over the 24 hours.

LYMPHOSARCOMA IN CHILDHOOD

A REPORT by Rosenberg et al.[1] from the Memorial Centre for Cancer and Allied Diseases, New York, re-emphasises the rarity of lymphosarcoma in childhood. The term "lymphosarcoma" is used to include all primary malignant tumours of lymphoid origin except Hodgkin's disease, and the cases have been divided into three groups: giant-follicle lymphosarcoma, reticulum-cell sarcoma, and lymphosarcoma. An attempt was made to exclude all patients with leukæmia, though it was realised that the criteria for this had to be arbitrary. Nonetheless, Rosenberg et al. believe that lymphosarcoma can progress "without showing significant bone-marrow involvement or abnormal cells in the peripheral blood". Of a total of 1269 cases treated at the centre in the past thirty years, 69 originated at 15 or less years of age. In these 69 the male to female ratio was 2·6 : 1·0; the male preponderance was even greater in patients aged 11–15 years. Certain differences between the childhood and adult disease were noted; in children presentation with abdominal symptoms, primary lesions in the small intestine, and bone lesions were all commoner than in adults. Bone lesions, usually solitary and painful, were the initial manifestation of disease in 4% of the 69 children—which is over five times the rate in the adult group. The condition was often more generalised in adults than in children, but in children the local disease was apt to grow very quickly.

Knowledge of the course of this disease in childhood is essential if treatment is to be effective. The New York workers make a plea for radical surgery where there is localisation to one group of lymph-nodes, to bone, or even to the small intestine. Of 8 patients, aged 2–13 years, who were operated on, 2 survived for ten or more years; but none of the other 6 survived for more than sixteen months. 8 further children survived for from four and a half to thirteen years after radiation therapy, or radiation combined with surgery or chemotherapy. Thus there was reasonably long survival in 10 of the 69 cases—nearly 15%. Among these 10 cases, it must be noted, were 3 reticulum-cell sarcomas of bone and 2 lymphosarcomas judged histologically to be of the least malignant type. Not all pathologists would accept reticulum-cell sarcoma of bone as a specific entity, though all would agree that children are subject to a local myeloid lesion of bone which is variously regarded as Ewing's tumour, secondary neuroblastoma, or reticulum-cell sarcoma.

It is salutary to be reminded that among the protean manifestations of malignant disease of lymphoid tissue (in its widest sense) is a less malignant group where recurrence after treatment may be long delayed or may not develop at all. It seems important that the experience of other centres should be analysed in similar fashion.

1. Rosenberg, S. A., Diamond, H. D., Dargeon, M. D., Craven, L. F. *New Engl. J. Med.* 1958, **259**, 505.

KOPLIK'S SPOTS

"IT is indeed very late in the day to describe something connected with the diagnosis of the exanthemata," said Koplik in 1896.[1] Born just a hundred years ago, on Oct. 28, 1858, he was 38 when he described his spots—having made his observations at the Good Samaritan Dispensary, New York. The first record of them is attributed to John Quier towards the end of the 18th century,[2] but the only observer whose description is generally known was the young Osler. From the first edition of Osler's textbook, published in 1892, Koplik quotes:

"Examination of the throat may show a reddish hyperæmia, or in some instances, a distinct punctiform rash. Occasionally this spreads over the whole mucous membrane of the mouth with the exception of the tongue."

The merit of Koplik's detailed account lies in his shifting the emphasis from the palate to the mouth:

"There is nothing especially distinctive about the eruption in the pharynx, or on the hard or soft palate in measles. The throat, in the beginning, is reddened, the fauces, the soft palate, may be spotted but this is also the case in many affections, such as grippe, Rotheln, catarrhal angina, and scarlet fever,"

and he goes on to add:

"On the buccal mucous membrane and the inside of the lips, we invariably see a distinct eruption. It consists of small, irregular spots, of a bright red colour. In the centre of each spot, there is noted, in strong daylight, a minute bluish white speck. These red spots, with accompanying specks of a bluish white color, are absolutely pathognomonic of beginning measles, and when seen can be relied upon as the forerunner of the skin eruption."

The spots have stood the test of time. Perhaps Koplik's statement that the enanthem always precedes the exanthem is open to question, but no-one doubts that the eruption is pathognomonic of measles. The only other clinical sign worthy of mention which has been described since 1896 is the "illness of infection of measles", which can be seen in some 10% of sufferers. Goodall gave the first account in 1925.[3] He noticed a few children who, after exposure, developed symptoms highly suggestive of measles, which disappeared in a day or two but were followed within the limits of the incubation by a typical attack. In his thirty-two years in a London fever hospital, Goodall saw 8 cases. Some of the so-called second attacks described before this symptom was recognised were nothing more than the true attack following the illness of infection.

1. Koplik, H. *Arch. Pediat.* 1896, **13**, 918.
2. von Goerke, H. *West Indian med. J.* 1956, **5**, 23.
3. Goodall, E. W. *Clin. J.* 1925, **54**, 69.

Special Articles

A HOSPITAL FOR THE PSYCHOTIC-DEFECTIVE CHILD

GERALD O'GORMAN
M.R.C.P., D.P.M.
PHYSICIAN-SUPERINTENDENT, BOROCOURT HOSPITAL, PEPPARD, NEAR READING

LACK of suitable accommodation for seriously disturbed and psychotic children, and the urgent need for research into psychosis in early life, led to the opening, three years ago, of a special unit where we could gather under one roof children with illnesses of every degree of severity, could treat them, and could observe results. In view of the suggestion (DeSanctis 1906, Kraepelin 1919, O'Gorman 1954) that juvenile psychosis may produce adult defect, and that many children and adults in mental-deficiency institutions are in fact psychotics with varying degrees of deterioration, we wanted to study the possible correlation between changes in emotional state and intellectual development.

THE HOSPITAL

Finding the right accommodation presented difficulty. An ordinary mental-deficiency hospital was not suitable because family doctors, medical officers of health, and parents might be unwilling to send psychotic or severely disturbed children there. We needed a hospital outside the Mental Deficiency Act to which children with severe emotional disturbance could be admitted for investigation and treatment with no more than a written request from the parent or guardian.

Fortunately suitable premises were at hand, for Smiths Isolation Hospital, Henley-on-Thames, had been taken over by the Oxford Regional Hospital Board and used to house up to 34 defective children as part of the Borocourt Mental Deficiency Group. It was decided that Smiths should become the unit for children with emotional disturbances associated with retardation.

The hospital had already been "designated" by the Minister as a mental-deficiency hospital; but after a good deal of discussion, in which the Board of Control as well as the Oxford regional board took a progressive and encouraging line, Smiths Hospital was (in December, 1955) "de-designated"—i.e., declared no longer to be a hospital for mental defectives within the meaning of the Mental Deficiency Act. The children already in residence were transferred to the parent hospital, Borocourt, for one day, and then licensed to the care of the Matron at Smiths Hospital. Since then children have been admitted simply upon the parents' written request and certification has been found unnecessary. (Under the recent change in procedure, a child can now enter any mental-deficiency hospital on the request of the parent; but in 1955 certification was still necessary.)

THE CHILDREN

As a rule children were admitted through the child-guidance and mental-deficiency clinics held in the region. Some had been notified or ascertained as mentally deficient before they were referred to the clinic, but this did not mean that they had to be certified before joining the unit. We notified the local authority of each child's admission.

Most, though not all, psychotic children are retarded below their intellectual potential, so that the functioning intelligence of our patients ranges from above average to the low-grade-imbecile level; the degree of disturbance ranges from "serious" to "very severe".

Age

At first we tried to admit only children of 5–10 years of age. But when clinical considerations forced us to admit older and younger children, we found that this repeated the normal family situation and that mixing the age-groups was beneficial rather than harmful.

Since the hospital has been opened, the doctors in the region have come to recognise potentially psychotic features in children at an earlier age, and more young children have therefore tended to be admitted. On the other hand, because the hospital must be organised so as to cope with impulsive or dangerous psychotics other institutions, such as schools for the educationally subnormal and general and psychiatric hospitals, have asked us to take older children with severe disorders. It has become clear that our chances of producing improvement are much greater if treatment can be started at an early stage of the disease; so the average age of patients tends to fall.

Clinical Types

In the early days we tried mixing seriously disturbed children with stable defectives in the hope, first, that the stable would provide an emotionally normal environment which might help the disturbed, and secondly that the defective child might be stimulated by contact with those of higher basic intelligence. We have dropped this policy because we have found it easier than we expected to provide a calm emotional atmosphere, and disturbed children as they improve are of great help to the more seriously disturbed new admissions. Moreover, there are now so many disturbed and psychotic children on the waiting-list that there is little room for the ordinary stable defective. The children do not fall easily into diagnostic categories; indeed, in assessing the pathology of a child's emotional disturbance, we often find it extremely difficult to disentangle the organic from the psychic side; and of course a firm decision is not always feasible. We therefore decided that no diagnostic category should be excluded, and we have admitted patients diagnosed as depressive, manic, schizophrenic, autistic, hyperkinetic, deaf, hysterical, psychopathic, and epileptic (various types), as well as those grouped under eponymous titles such as Kanner's syndrome and Heller's syndrome. The criterion for admission is that the child shall be seriously disturbed, but we give preference to those in whom emotional disorder seems to be causing intellectual retardation.

ORGANISATION AND TREATMENT

Schooling

The hospital has its own school, with two teachers, which nearly all the children attend for 3–5 hours a day. The size of the classes is kept to about fourteen. In placing the children compatibility has to be taken into account, as well as the educational attainment. Much of the teachers' time has to be spent in semi-recreational activities, including singing, dancing, and eurhythmics, because most children are unwilling to do school work for more than short periods. Consequently the standard of work is not very high, and it cannot be much raised till we can afford to have several more teachers.

On the other hand every child's educational attainment is much higher after a few months at the school than it was before he came in. The discipline in the school is rather firmer than in the hospital as a whole, but the child goes into school only if he wants to, and he may leave if he feels so inclined. Very few do so.

Physical Training

More emphasis is laid on handicraft training than in an ordinary school. The children have orthodox physical training and eurythmics, but it is hard to get them to play organised games. The hospital has many domestic animals, for some of the psychotic children find it easier to form a relationship with an animal than with a human being. Motor-car rides and river trips are by and large the children's favourite recreation. Our therapeutic aim is to try to ensure that the child shares an experience in some measure with another human being.

Nursing

The hospital is run as a matriarchy, with the matron at the head. There are two ward sisters, each of whom has a number of nurses responsible to her. Each nurse has her own team of two nursemaids and four children. Each nursemaid is responsible to the nurse for two children.

Social Work

Childhood psychosis is of course a family problem. We have to try to discharge the child to a normal family environment, whereas almost always he has come from a disturbed home, a depleted home, or no home at all. We have rarely found a psychotic child whose mother was not emotionally disturbed—some are disturbed so much that they need psychotherapy for a long time—and obviously the child's psychosis, be it organic or psychogenic, must reciprocally affect emotional relationships in the family. If the parents refuse or are unable to cooperate, or if there are no parents, then we have to find parent substitutes. All the social work that this entails is done, in cooperation with the children's therapists, by two psychiatric social workers, working part-time with the families of Smiths Hospital children. Here again we need a larger staff and many parents need medical psychotherapy instead of, or as well as, the help of the P.S.W. An obvious need is for group-therapy of the parents, but owing to difficulties of travel and medical staffing this has not been arranged.

THERAPY

The ideal in treating these seriously disturbed children is that each shall have intensive psychotherapy coupled with such physical treatment and occupation or schooling as his condition warrants.

A few children have improved temporarily on drugs of the chlorpromazine and reserpine groups, and dextroamphetamine has been very helpful to several, often in combination with the barbiturates. We used electroconvulsion therapy for a few children to begin with but quickly abandoned it. We used leucotomy three times, but it was not so effective as to overcome our aversion to it except in the hope of reducing the misery of apparently hopelessly deteriorated children.

The chief form of treatment must be psychotherapy. But we have only three physicians and two psychologists—all part-time—who practise psychotherapy. Moreover, it became increasingly clear that, to be effective, therapy has to be very intensive: indeed it almost seemed that each child required half a doctor and one nurse to himself. At first therefore we made a virtue of our inadequacies by selecting, by lot, the children who were to receive psychotherapy, leaving the others as controls. Even so, sessions twice weekly were as much as we could attempt, and even these were curtailed by holidays, illnesses, and conferences. Without more medical staff it was obvious that the treatment of even these few children was going to be inadequate. A therapist could spend no more than, say, six hours a week with a particular child—and this at the expense of the other patients. Indeed, from the standpoint of the community as a whole it would hardly be justifiable to treat any child in this exceedingly expensive way unless it showed promise of real genius.

BIG SISTERS

We already knew that the prime difficulty of the psychotic child was in forming emotional relationships. Everything turned on the therapist's being able to get into some sort of rapport with the child. Hence a therapist who found it easy to establish a warm relationship with the child would be more successful than one who (though perhaps more intelligent) had less ability to form such emotional ties. We knew that verbal interpretations based on analytical formulations would cut little ice with the psychotic children—they would not be listening. Intuitive understanding and an ability to enter a little way into the child's emotional world seemed to be the essential tools.

Now this ability to get into rapport with a psychotic child is by no means confined to psychiatrists and professional therapists. It seems to be a gift—or perhaps a quality—which no amount of training can confer, though training improves the use one can make of it. Faced with our shortage of staff we decided that if we could find people with this quality psychiatrists might be able to treat a child through their agency. The obvious people were the nurses. We therefore tried to train the nurses, who were, after all, on the spot most of the time, to carry out most of the treatment under medical guidance. The idea was that one doctor would supervise the work of several nurses, explaining the psychopathology in appropriate terms, and directing the nurse's approach and methods of handling. But this policy was only partly successful, because we had not enough doctors and nurses, and because it was hard to find nurses with the right qualities. We have only 10 nurses altogether, and at first many of them were student and part-time nurses whose relation with the children tended to be interrupted by off-duty, lectures, and transfers to other departments. We therefore replaced student nurses by assistant nurses who could work whole time. Even the most suitable nurses or assistant nurses were not engaged unless they were likely to stay permanently.

But our chances of helping the children seemed to depend directly on how much individual attention we could give them, and it was difficult to see how we could progress without a great increase in staff. We therefore tried the experiment of using " big sisters " as unskilled aides to the nurses. These big sisters are high-grade mentally defective girls from a neighbouring institution, who came daily to Smiths Hospital.

They are given training in domestic work and in looking after the children. At the same time they will, we hope, provide some of the maternal affection which the children need. We try to assign one big sister to each pair of younger children, which means that we have a large number of domestics so that the big sisters can spend about half their time playing with their charges or taking them for walks and generally caring for them—all under close supervision by the nurses. It is too early to assess the results of this system, but most of the children take to their big sisters in a most gratifying way, even though the relation seems at first to be purely physical. The great virtue of the big sisters seems to be that their affection is undemanding: for so many of the psychotic children have come from mothers who are themselves tense, remote, or rejecting. However, the big sisters are of course mentally defective patients, and continuous supervision and encouragement has to be given them by the nurses.

RESULTS

A detailed assessment of our results is not yet possible, and we can offer only some general impressions. Though we are taking in 13% more patients than originally intended, our waiting-list has grown at a rate which suggests that our approach is finding favour with local health authorities, family doctors, and pædiatricians.

When we took over we kept 15 of the original patients, 3 of whom were regarded as psychotic. They have all since been transferred to mental-deficiency hospitals. Of the 105 patients we have admitted:

27 have been transferred to mental-deficiency hospitals,

7 have been transferred to residential or day schools for E.S.N. children.

9 have returned to the normal school system or to normal community life.

14 have returned to their own homes after temporary admission.

3 have been removed against our advice.

The least severely affected children have been the quickest to improve. Those admitted for depression or for severe neurotic upset have improved more than schizophrenic or epileptic patients, and those with early schizoid deviations have of course improved very much more than those with chronic deteriorated schizophrenia. In the schizophrenic group, even when we could coax a child back into apparently normal emotional relationships, it was disappointingly difficult to increase his intelligence quotient. In many cases we have had to be content with a reasonably stable and undisturbed child functioning intellectually at a level several years below his chronological age. Such children scored best on tests of social attainment, and worst, in general, on written and verbal tests.

Another disappointment was the long time needed to produce real improvement in schizophrenic children. We started off with hopes of doing wonders in a year or two, even with severely psychotic children. We now realise that we must be prepared to keep such a child, if necessary, for the whole of his school life. On the other hand, experience has taught us that even when a child shows little improvement after several years at the hospital, he may suddenly begin to talk and to form normal emotional relationships at the ripe old age of 8 or 9 years. We found it easier to treat children whose environment had contained gross precipitating factors than those whose environments and upbringing had been fairly normal, and whose illness, we suppose, must therefore have a proportionately large constitutional element.

We also found it much easier to treat very small children than children of 7 or more years of age. For this reason, in choosing those to be admitted, we now tend to give priority to 2-year-olds and 3-year-olds.

CONCLUSION

Twenty years ago active treatment of adult psychotics was usually held to be largely ineffectual. Since then the outlook has changed, and the atmosphere in most mental hospitals is now therapeutic rather than custodial. In the mental-deficiency hospital, however, the old custodial attitude lingers: indeed the word "institution" or "colony" is often used rather than "hospital".

In the future the emphasis in the mental-deficiency hospital should be on prevention, treatment, and training rather than on segregation and basic nursing. If adult psychotics can be treated, then we must make a determined effort to treat those juvenile psychotics who, untreated, must become part of the long-stay population of the mental-deficiency hospital. Since we are largely in the dark about the pathology of juvenile psychosis, our early steps in search of appropriate treatments must be halting. Smiths Hospital is designed to be one of the first of these steps.

REFERENCES

DeSanctis, S. (1906) *Riv. sper. Freniat.* **32**, 141.
Kraepelin, E. (1919) Dementia Praecox and Paraphrenia. Edinburgh.
O'Gorman, G. (1954) *J. ment. Sci.* **100**, 934.

The Widdicombe File

XLIX. BENEFIT OF PARKINSON

DEAR JAMES,

But you must read *Parkinson's Law*! I know you're a busy man, and I know the Senate are counting on your keeping your golf in the groove against the next match against our Northern colleagues; and I know too that, being more skilful than most of us at manipulating bureaucracy for your own ends, you are the less tolerant of uninformed criticism of the bureaucrats. But the book has become part of the mythology of literate Britain, and you cannot altogether neglect it. You cannot even defend yourself by claiming never to read anything while it is fashionable: it is a few months now past its peak of popularity, and to read it now might give you, on the micro-scale, something of the same recherché satisfaction one can get by consistently and pointedly reading the works of authors just past their first flush of extreme favour—Kafka, say, or Joyce or 'ginia Woolf to take a random current sample—whom it is already more fashionable to have read than to be found actually reading.

One of the oddest things about the book, to anyone interested in today's mythology, is that the aphorism which is widely quoted as Parkinson's Law isn't (according to Parkinson himself, who should surely know) Parkinson's Law at all. It is in fact the first sentence of the first chapter (leading to the unkind thought that most reviewers must have read no further); but it is the beginning of the argument, not its conclusion. Parkinson's Law, as enunciated, is merely the statement that Government departments have a built-in constant rate of increase (about 5·7% per annum compound) which is independent of the demands made on the department. That may well be true, and if true may well be important, but it has little entertainment value. What Parkinson makes entertaining, and what has caught the public fancy, is the argument put up to explain the increase. This begins by postulating that

> "Work expands so as to fill the time available for its completion"

—the phrase now universally hailed with glee as Parkinson's Law. The full argument you must study in the original: roughly speaking it points out that the conscientious worker is always busy, so no department is ever understaffed, and that expansion of staff, once begun, increases the endogenous work resulting from interpersonal and communication problems so that expansion breeds expansion.

Accepting for the moment the expanded pseudo-law as a real thing—and one must admit its wide acceptance points to a seasoning of truth in it at least—it is worth seeing just how far the cap fits people like us. Our own department has just added a new lecturer, and is already angling for another. I would not hold you altogether innocent of similar designs yourself; and indeed where, up and down this whole school, will you find a live department that isn't up to the same game? Yet our annual through-put of students is if anything falling a trifle, and the hospital is little bigger than it was ten years ago. Does then Parkinson's Law apply to us—to hospital departments and university departments, as well as the

Civil Service? Do we expand because expansion is an inherent characteristic of the organism, regardless of whether there is a real demand for our services?

Of course we do! Every university department, every hospital, firm or unit, regards expansion as the natural order of things. Who ever heard of a professor who had too many lecturers, a surgeon with too many registrars, or, come to that, a sister with too many probationers? A new chief is as infallible a stimulus to multiplication as a spermatozoon to an ovum. Departments shrink only when they bud off new departments, and the progeny grow faster than ever. Parkinson's Law certainly applies to us. But does it matter? It seems to me that a major fallacy in Parkinson's (and the world's) interpretation of his law is the implicit assumption that it is a bad thing. That is a conclusion that ignores (most inappropriately, in this Darwinian year) the intra-species variability of man. We are variously made, and in no respect more so than in our attitude to what constitutes a good day's work. Between the old soldiers whose idea of a right job is immobility in brass buttons (with an assistant to polish the buttons), and the Nightingale types who are prepared to sacrifice not only their own comfort and their families', but the whole basis of their society, for the right to work unpaid eighteen hours a day in a pigsty, there are infinite gradations. Given a job—like many Civil Service posts, most university posts, and even (let's be honest) some N.H.S. posts—whose inescapable duties can be completed in a good deal less than a full working day, the possible reactions are endless. Some frankly scrimshank; some waste their time with conscientious fritterings; some, like Trollope, do a second job in their spare time; some devote themselves to saving the time of their colleagues by achieving the necessary minimum of efficient internal administration; but the ones who matter, the leaven in the lump, look round for real and relevant work to fill out the windfall of time presented to them. In the Civil Service that perhaps means just bigger and better memoranda: in the universities it means research: in the N.H.S. it may mean just doing that little bit extra for one's patients or—the same thing in the long run—it may also mean research.

Pure research jobs proliferate nowadays (not unalloyedly to the advantage of research some think) but even nowadays most research is a spare-time occupation. Rich eccentrics like Boyle and Darwin, successful technologists like Stevinus and Franklin and Joule, priests like Spallanzani and Mendel, practising physicians like Harvey and Malpighi and Thomas Young, Government officials at all levels from Bacon to Leeuwenhoek—all played their part. But nowadays by far the largest proportion of the part-time researchers are university staff (who, as the cant phrase goes, are *required* to teach and even now only *expected* to research). Basically, this depends almost solely on the university's ability to appoint able people, and not to overwork them on routine duties. Why does it not overwork them? Because by a continuous process of gentle expansion the university's staff keep just comfortably ahead of the necessity of doing a full day's routine work. And that gentle expansion is simply Parkinson's Law at work.

I have heard it said, and I believe it, that if penicillin had been exploited commercially to the full from the start (which God forbid) it would have paid many times over the entire cost, capital and current, since 1930 of every medical school in the country. It is expedient that a hundred professors should be stretched on the rack of a too easy chair, and drowned in interminable cups of tea, in order that one should have leisure to fiddle with a plate that might well have been flung in the lysol bucket if he'd been busier, and that ten years later another should have leisure enough to consider trying a long shot on making something useful out of this apparent sideline. It all comes from the application of Parkinson's Law. Long may it flourish!

This is just the first chapter. There's a lot more. But, as I said, the critics seem to have read only the first paragraph. Professor Parkinson professes history in Singapore, and some of his chapters are relevant only to such distant parts of the world. Such for instance as his life history of the genus Chinese millionaire, helpful only in those parts of the world where Chinese millionaires are common, and his stratigraphy of cocktail parties, which is I think based on Colonial practice. His chapter on the motivation of the financial decisions of committees, who pass millions without a murmur and fight over sixpences, is excellent: but Shaw has it all in a sentence in the preface to Heartbreak House.

Two things I think worth enlarging on. First is a very fine chapter on committees, showing how closely their efficiency inverses with their size. Again the cogency depends not on the conclusion, which is original only in its precise figures, but in the supporting statistics, with a most plausible relation of the effectiveness of Cabinets, ranging widely in geography and history, to their size. Evidence is produced for the figure of 12 as the maximum size for real effectiveness, and 21 for the limit above which the body collapses into total hopeless muddle, so that if its function is essential it can survive only by developing a central smaller nuclear body which does the real work (and, of course, in its turn the nucleus grows over the years and becomes ineffective, and a nucleolus is born to do the work of the nucleus, and the nucleolus grows in its turn till . . . so on and so on). Obvious enough—but have you noticed how Faculty is growing? Every year or two we have a new chair, and each new professor is on the Faculty, and so the Faculty grows without anyone noticing, and it gets harder and harder to get anything done. A curious and unexpected consequence of the growth of schools and the equality of professors.

Parkinson has also a most original plan for lightening the load on selection committees. He suggests that advertisements should be just sufficiently explicit on the *dis*advantages of the post to frighten off all the dead wood of applicants, and claims that an exactly gauged advertisement will attract just one applicant, who must be the right man. Perhaps there's something in it: can I venture a draft substitute for the recently advertised chair of pathology at St. Ethelred's?

The senate . . . invite applications, &c., &c. Duties . . . to include teaching of pathology: but it is to be clearly understood that this hospital disapproves of pathology as a separate subject, and students will be permitted to attend only when their duties in the wards and playing-fields allow. Research will be expected: a microscope is available, and the fitting of a sink in the professor's room is to be allowed for in the next quinquennial estimates but two. Present second-in-command an applicant: he will not be appointed, and is likely to resent this. He is an international authority on age changes in the organ of Zuckerkandl, and has confined his professional activities to giving papers on this subject for the past ten years. Remainder of staff incompetent, immovable, and not on speaking terms. No new appointments possible in the foreseeable future. During the past fortnight most of the departmental accommodation has been occupied quietly by the

dean's third secretary, several biochemists, a housekeeping sister, and the secretary of the rowing club, and this arrangement has proved to be so convenient that it is likely to be confirmed as a permanency by the Academic Board before the new appointment is made. Forms of application for the traditional ducking in the Thames at Tower Bridge may be obtained from the entertainments secretary of the S.R.C.

Perhaps it would lower the tale of applicants. And then again it might not. That is one net that is never vainly spread before the eyes of the birds: Parkinson has not allowed for the universal suckerhood of us mortals this time. But read him all the same, James.

Yours,
PETER DAVEY.

Parliament

The Queen's Speech

THE Queen's speech at the State opening of Parliament on Tuesday announced a wide programme of domestic legislation which promises an unusually busy session. A national superannuation scheme is envisaged, on the basis of the recent white-paper, " enabling a larger section of the people to build up pension rights related to their earnings ". A new Bill will be brought forward to replace existing legislation concerned with mental health. The Government " views with gravity the increase in crime " and hopes " to improve the penal system and to make methods of dealing with offenders more effective ". New proposals will also be made for the development of schools, " intended, in particular, to improve the scope and quality of secondary education ".

Public Health

Prevention and Home Care

THE two main trends in the National Health Service to which the Minister of Health drew attention last week, are (1) an increasing emphasis on prevention and (2) a growing recognition of the importance of home care. He was addressing the annual meeting of the Executive Councils' Association.

Under the heading of prevention, he mentioned that up to the end of August 5¾ million people had been vaccinated against poliomyelitis. In continuation of this work the help of family doctors was more than ever necessary, because the programme now included young adults, many of whom were likely to turn to their own doctors for vaccination. An all-out effort to raise the vaccination-rate among children and expectant mothers was also needed.

Fluoridation he described as " a measure of inestimable potential value in reducing dental decay ", which had the full support of the Government. " When the fluoridation demonstrations, which are now in progress in a number of areas, have gone a little further in showing what can be achieved and how, I hope we may look forward to advancing in this field on a broader front."

Dealing with home care, the Minister said that " the highest priority which the available funds allow should be given to helping old people to remain as long as they can in their own homes ". As for the mentally handicapped, they should be regarded in the same way as the physically ill or handicapped, and hospital care provided only for those who need hospital treatment or constant nursing care.

In England Now

A Running Commentary by Peripatetic Correspondents

As well as being members of two professions, the officers of the Army Medical Services seem all to be accomplished classical scholars. The Director-General's annual exercises are based upon episodes in ancient Greek mythology, and this year our attention was directed to Meilanion, who (according to the exercise instructions) defeated the swift-footed Atalanta in a race by distracting her with golden apples and then (according to my classical dictionary) became her husband.

We were a cosmopolitan company, representative of the Commonwealth countries, the NATO powers, and that country which perhaps more than any other lies midway between the great power blocs—Yugoslavia. The troops taking part included Gurkhas and a petty officer of the Royal Norwegian Navy.

A famous Territorial unit showed us how quickly the soldier can be taught to set up intravenous drips and pass Ryle's tubes, and did it in a field which was literally under water. (When *will* the rain stop, and *do* the bomb-tests have anything to do with it?) We were given a vivid forward glimpse of the day when (we hope) the helicopter will become the ambulance-car and the three-ton truck of the Army. There was a brilliant symposium on the varieties of viral encephalitis in South-East Asia, which provoked the lengthiest question that I have ever heard asked at a medical meeting.

A senior Army medical officer, who has travelled much, told me that there are three respects in which our Army Medical Services excel those of other countries: the quality of our military surgery (rivalled only by the French), the possession of a first-rate Army Nursing Corps, and our expertness in hygiene and preventive medicine. Yes, indeed. While the local authorities seem cheerfully content to see the public-health service pass entirely into non-medical hands, the Army showed us the vital services which its hygiene specialists could perform for the civilian population if ever this country became a theatre of war.

We discussed the disposition of medical units on the nuclear battlefield; we chatted; we ate and drank together. (Yugoslavian wines were provided for the exercise supper, and one or two of us sampled the Yugoslavian hangover.) We renewed old friendships and made new ones, and indulged in all the other extracurricular activities which are the most fruitful part of any conference, military or civil. Isn't it a pity that Somerset House has never grasped this point?

* * *

I have spent this still, bright, autumn Sunday morning mowing an overgrown lawn with a scythe and I feel all lyrical about the thing. Its lovely shape was clearly not devised either by one or a series of inventors but has evolved, as surely as the gull's wing, which it rather resembles, or like a folk-song, under the hands of generations of mowers until it has reached perfection. No machine, I am sure, could make it.

In use it pleases all the senses at once. The smooth, wooden handles (ash, I fancy) are good to feel in the hands; it sounds good, whether cutting or being honed; one can't actually taste it, but I needn't dilate on the smell of cut grass (mixed this morning with fallen leaves and a touch of bonfire); if rhythm be a sense it is satisfied, and the same goes for accomplishment. Ten tireless shearers on their knees might perhaps do the work of one elderly doctor on his feet, but they wouldn't have enjoyed themselves or want their lunch as he does. Of course one of these repellant, oil-driven, whirling-blade machines, towing its owner-driver and giving its famous imitation of Blake's old Nobodaddy aloft, might do the work in a quarter the time and, in terms of invested capital, at quite ten times the cost; but I think it would have excoriated the ground.

But one strange footnote must be added. On the haft of my loved and lovely scythe, bought new in an English county town some eighteen years ago, is a label with the maker's name

and the words " made in U.S.A." *O tempora!* Well may I direct my little outburst to the column headed " In England Now ".

• • •

Men with blues never came to my hospital, because the hockey team wasn't good enough. The viciousness of the circle thus produced left us with one erratic side that felt pleased with itself when its opponents' score was kept below double figures. We used to write apologetic letters in advance to clubs on our fixture-list and they were terribly sporting about it, or perhaps they went on playing us year after year because it made their goal-averages look good, I don't know. Anyway, we reckon we had the most practised if not the most skilful goalkeeper in the southern counties.

Longer ago than I care to recall, when I came up as the freshest of fresh clinical students, I was hailed as the only new man to have played before and made captain. The previous season's matches had ended at Christmas with a row after which half the team refused to play with the other half. However, I gathered together some whose egos weren't too badly frayed, and with some willing if hamhanded tyros we took the field. Scoring goals was out of the question so we packed the defence. No side got more than 17 against us, which only works out at a goal every 4 minutes. The next season we won once, and by the time I left, double-figures had become a rarity.

So it was with much satisfaction that, after a six-year absence I went back to play for the old place again. Young chaps way below and barely known to me were now regarded as legendary figures of the past: memory of me was quite lost in the mists of antiquity which was saddening because I'm not thirty yet. The team is a lot better now (or else I'm a lot worse). I was reassured, though, by one of our old opponents who told me that when he started playing for his club half his team hadn't been born. He asked me what had happened to that young chap that used to play centre-half for us, got married, brought his kiddie along, and finally went overseas. I was pleased to tell him I was keeping well.

• • •

When the leaves begin to turn, my wife disappears into the domestic equivalent of the sterilising-room. Steam and a variety of smells penetrate the rest of the house, and in due course the top shelf of the pantry accumulates bottles and jars of preserves. This year the apples have cropped well, but there are no pears. One plum tree has contributed four rich red jars to the row. The raspberries were too sodden to bother about, and something happened to the gooseberries and currants. " It's just as well," she sighs. " Isn't it a blessing when *something* is a failure? " I read a little homily to her; for we have not always been in a position to harvest our own fresh fruit.

My house-surgeon meets me on the steps of the hospital. " There's a gastrectomy, sir, but the gallbladder hasn't come in. And the colectomy case had a transfusion reaction last night, so I've put him off." " Thank goodness for that," say I; " now I'll get home in decent time for lunch." Then I think of my wife and the fruit bottles, and wonder what sort of a *tu quoque* I'll get at the end of the morning.

• • •

I was lately uplifted by the gift of an altimeter for my car, but it will be necessary to do some high Continental driving to obtain proper satisfaction from this gadget. On my daily run in to town the dizzy heights of Hampstead are barely indicated, but I was somewhat astonished to find that my garage must have risen almost 1000 feet in one night last week. Going back to my student days I remember being taught that for every 1000 feet in height, the barometer falls about 1 in., so that until the season for mountain climbing comes around again my new possession is in fact a portable barometer in reverse. For every barometric rise of 1 in. the machine registers a fall of 1000 feet and similarly a fall of 1 in. is registered by a rise of 1000 feet.

Letters to the Editor

FUTURE OF MENTAL-DEFICIENCY PRACTICE

SIR,—Mental-deficiency practice has been too long shrouded in legal formalities and legal jargon.

It has tended to use such quasi-legal terms as " mental defective ", " feeble-minded ", " imbecile ", or " idiot " as though they had some diagnostic significance, though they have in fact no medical authority at all. Doctors and nurses spend too much time repeating to the Board of Control such statements as " He is an imbecile ", " He is clean only under close supervision ", " He cannot read or write ", " He is unable to name the days of the week and is unable to give an account of his past ", " He has an I.Q. of 40 and requires nursing supervision for his daily welfare ", or " He is an epileptic in fair health ". Such statements are of little use from a medical standpoint. They always say what the patient cannot do and never give an account of what he can.

The new procedure for the admission of patients to mental-deficiency hospitals gives us an opportunity to drop this legal terminology, and to begin to group our patients, not according to their legal category, but according to the ætiological diagnosis of their condition. Admittedly in the present state of our knowledge it is not always possible to define the ætiology of a disorder, but until we begin to look at each patient as a medical problem little progress will be made, and the tendency to accept mental defect as " an act of God " about which little can be done, and—what is worse—the feeling that it is not even worth trying to do anything, will be perpetuated. Studies on the metabolism and biochemistry of the defective have thrown light on phenylketonuria, galactosæmia, hypercalcæmia, and the Reeves syndrome, and have shown how much the biochemist, the endocrinologist, and the neurologist, as well as the geneticist, psychologist, psychiatrist, and general physician, have to contribute to this specialty.

Once it is realised that mental deficiency is a medical problem though a tough one, mental-deficiency practice will emerge as a specialty in its own right. Its present association with psychiatry is unrealistic, and a change in terminology and a shift of emphasis would allow mental deficiency to be separated from acute mental illness and to be presented, as it is, as a specialised developmental failure.

Ottershaw, Surrey. GORDON DUTTON.

SEPARATISM OR REINTEGRATION?

SIR,—As one who has been interested in the M.R.C.P. examination for many years, may I be allowed to comment on your leading article of Oct. 18?

You greatly exaggerate the difficulty of graduates who are specialising in some non-clinical subject in passing the M.R.C.P. Such a view is at variance with the actual results. I have successfully coached many pathologists, radiologists, psychiatrists, &c., for this examination, and in every pass-list these groups are well represented. In fact, I would put the chances of an intelligent (and perhaps lucky) fellow who is doing pathology higher than one who is engaged wholly in clinical medicine. Such candidates are much more likely to have their feet on the ground, to be self-critical of their clinical abilities, to possess clinical humility and not to boast, for example, of the many wonderful things they can hear with their guessing tubes. Recent results from a London teaching hospital are typical.

Of the 8 registrars and S.H.O.s taking the examination the successful 3 were registrars in pathology, radiology, and psychiatry, and the unsuccessful 5 were all doing clinical medicine. Such results are very common.

Moreover, whether it be an agreed policy of the College or not, the fact is that the clinical cases shown are becoming easier and more elementary and this also favours such candidates as pathologists. Many successful candidates have had clinical cases of the following pattern: a straightforward heart lesion as a long case, and as short cases, for example, an enlarged spleen for discussion of likely causes and investigations, an arthritic for differential diagnosis and investigations, and an endocrine disease for spot diagnosis and full discussion of investigations. With such a clinical examination I would back the intelligent pathologist who has had sound basic elementary clinical teaching against any candidate who has spent several years in the rarified atmosphere of some of the medical units.

Has not the pathologist other higher qualifications open to him? In the Edinburgh M.R.C.P. pathology can be taken as a special subject. The London M.D. was once a very good clinical examination but is now a research qualification, and a pathologist, especially if attached to a teaching hospital, is more likely to write a successful thesis than a registrar engaged entirely in clinical medicine.

You dismiss lightly the possibility that somebody who has obtained a M.R.C.P. in a special subject would later obtain a consultant post as a general physician. But this has happened and I know of at least 3 such people. But the most naïve statement is that "it is inconceivable that anyone—were he M.R.C.P. three times over—would be appointed as a clinical consultant unless he has proved his clinical ability in many years of hospital practice". I would advise you to analyse the appointments to posts of general physicians made during the past ten years to London teaching hospitals and the Metropolitan regional hospitals. You would then be surprised at the considerable number who have had very little clinical experience but have spent most of their postgraduate life in departments of pathology or physiology. In fact the recognised way to jump the consultant-physician bandwagon is to avoid clinical experience as far as possible and to concentrate on physiological or pathological research or even statistics, and the more abstruse the subject the better.

London, W.1. M. H. PAPPWORTH.

MOTHERS WITH CHILDREN IN A PSYCHIATRIC HOSPITAL

SIR,—The article by Dr. Main (Oct. 18), describing how he has taken children with their mothers into the Cassel Hospital, is very welcome. On a number of occasions during the past two years at this hospital, psychiatrically ill mothers have been admitted to our mothers' room in order to prevent the sending of a baby to a residential nursery while the mother is sent to a mental hospital. It has been practicable to arrange for the mother to continue under supervision of, and when necessary treatment by, a psychiatrist. We have felt that while a mother goes through, for example, a depression it is valuable for both mother and child to keep in contact with each other, as otherwise they tend "to grow apart" and potentially another mentally sick person is nurtured. It seems especially important to try to keep the mother-child relationship satisfactory when "the soil" is poor.

These trial admissions have been made with the co-operation of the matron and nursing staff, who have felt that the apparently beneficial results have made them well worth while. As, however, in our experience the desirability of such joint admissions when the mother is mentally ill is not infrequent, and hospitals taking adult mental patients are probably more easily adapted for having babies within their walls than children's hospitals for mentally ill parents, one hopes that Dr. Main's experiment will not remain too exceptional.

Paddington Green Children's Hospital, London, W.2. THOMAS STAPLETON.

EARLY DIAGNOSIS OF CRETINISM

SIR,—Your important annotation of Oct. 25 failed to mention the association between prolonged "physiological" jaundice and congenital hypothyroidism that was described by Åkerrén [1] in 1954. He reported three such cases of his own and seven more that had been seen by others. Subsequently Christensen [2] reported eleven infants with congenital hypothyroidism, five of whom had had jaundice of more than two months' duration after birth, and Amlie [3] reported that six out of twenty-four cases of congenital hypothyroidism had had "icterus neonatorum prolongatus".

I have under my care a child, now aged seven months, who became jaundiced three days after a normal full-term birth. As the jaundice was still present at the age of one month she was admitted to hospital with her mother, and full investigations were carried out. There was no evidence of increased hæmolysis, of biliary obstruction, or of any metabolic disorder. No diagnosis was established and the jaundice persisted, but as the baby was otherwise thriving, and was successfully breast feeding, she was discharged to outpatients. At the age of seven weeks she was still slightly jaundiced (total serum-bilirubin 3·0 mg. per 100 ml.) but now showed evidence of hypothyroidism in that there was puffiness of the face and neck, enlargement and protrusion of the tongue, a dry skin, and an umbilical hernia. She was started on thyroid gr. $^1/_4$ daily and in two weeks the jaundice had cleared but her appearance was still cretinoid. By the age of four months her appearance was almost normal and her developmental progress was satisfactory. At five months the thyroid was discontinued in order to confirm the diagnosis and after a few weeks there was a marked change in temperament and appearance. She was difficult to feed, constipated, had coldness and blueness of her extremities, and her face was becoming puffy again. The serum-cholesterol, which was 160 mg. per 100 ml. at the time that thyroid was discontinued, did not rise significantly after a month without treatment, although there was a reversal of the ratio of the free and esterified fractions. She has since resumed treatment and there has been a rapid improvement in her condition. Her developmental level is normal.

Severe or persistent jaundice in the newborn infant is a fascinating diagnostic exercise as almost twenty distinct causes are now recognised and, even then, some cases defy classification. The possibility of hypothyroidism should always be considered and confirmatory signs sought if no other cause of the jaundice can be found.

Finally, Sir, I cannot accept your condemnation of thyroid administration as a therapeutic test. The response to thyroid in non-goitrous cretins is nearly always so clear-cut as to leave little room for doubt. Occasionally, as in my own patient, interruption of treatment so as to confirm the diagnosis may be justified and the subsequent change is equally striking. There is no evidence to suggest that temporary interruptions of treatment affect the prognosis. Of the alternative methods of diagnosis that you suggest, estimations of protein-bound iodine are difficult and fraught with error, ^{131}I-uptake studies are potentially hazardous,[4] ^{132}I is very short-lived and its

1. Åkerrén, Y. *Acta Pædiat., Stockh.* 1954, **43**, 411.
2. Christensen, J. F. *ibid.* 1956, **45**, 367.
3. Amlie, R. *ibid.* 1955, suppl. 103, p. 58.
4. Hubble, D. V., Hutchison, J. H., Evans, P. R. *Arch. Dis. Childh.* 1957, **32**, 166.

use is therefore limited. The therapeutic test is both simpler and safer than any of these, provided careful observations are made. Whilst fully aware of the enormous contribution to medicine by laboratory investigations we should not allow them to blunt our clinical judgment.

Alder Hey Children's Hospital, Liverpool. S. E. KEIDAN.

"FALSE" SICKLE CELLS

SIR,—In your issue of Sept. 6, Dr. Caminopetros and his colleagues revive the controversy regarding the nature of the "false sickling" phenomenon. They assert that "the sickling observed, though slow and limited, is genuine and not false as has been suggested" and that "false sickling has so far been observed only in people who exhibit the trait". Evidence exists to refute both assertions.

At the 5th International Congress of Blood Transfusion in 1954 I presented a paper on the subject of "false sickling" [1] and also an exhibit consisting of numerous photomicrographs demonstrating the various aspects of this phenomenon. As Caminopetros et al. have omitted this paper from their references, I must assume they are unaware of it. May I, therefore, reiterate the main findings of this study and so perhaps lay the ghost which has for so long haunted true drepanocytosis in the pages of your journal.[2]

Using specially cleaned glassware, sealed wet specimens of 2% blood suspensions in 1% 'Normosal'* were made twice weekly for eleven consecutive weeks from 24 members of the technical staff of the South African Blood Transfusion Service in Johannesburg. 18 were females and 6 were males. All were of unquestionably pure Western European stock and none showed any abnormal hæmoglobins on repeated electrophoretic studies. With only 1 exception—a spinster aged 42 years—false sickling was observed to occur regularly in the females throughout the luteal phase of the menstrual cycle, becoming maximal just before menstruation and disappearing rapidly after the onset of bleeding. False sickling was also observed on occasions in all the males but less frequently than in females; the number of distorted forms was fewer and there was no suggestion of cyclical periodicity.

The phenomenon was shown to be due to the formation within the body of the cell of one or more straight, highly refractile filaments which increase in length up to as much as two or three times the normal cell diameter. The envelope of the cell becomes extruded to accommodate the lengths of the filaments and the cell shape becomes correspondingly distorted. Depending on the number, direction, and length of the filaments, the cells may assume any of a variety of angulated forms. Most frequently, there are only one or two parallel or superimposed filaments in which case the cell becomes elongated and lenticular in shape (fig. 1). Should these filaments bend or break within the body of the cell, the lenticular forms become converted into crescents. If one of the filaments diverges markedly from the other, the cell becomes bifurcated at one or both ends. (The filaments and corresponding shape changes are in fact also distinctly and typically shown in the upper section of fig. 3 of Caminopetros' own paper.) When there are numerous filaments criss-crossing through the body of the cell, the latter assumes a polygonal shape which may be mistaken for the holly-leaf form of true sickling. Fig. 2 shows the great variety of forms which may be observed in false sickling in human blood.

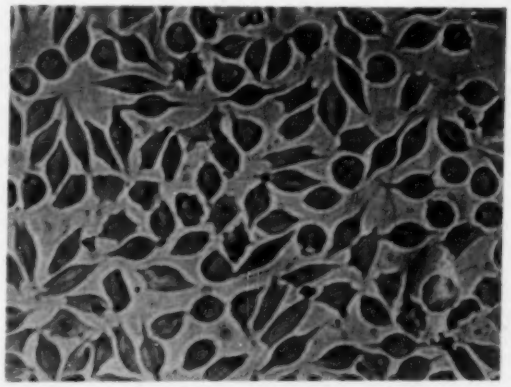


Fig. 1—False sickling: predominantly lenticular forms in human cells.

Because the formation of filaments or spicules is the essential feature of false sickling, I suggested the use of the term "spiculated cells" to distinguish such cells from other well-recognised shape changes (e.g., sickle cells).

The spiculated cells begin to form in eight to twenty-four hours from the time of preparation of the sealed wet specimen, appearing usually in one or more areas along the margin of the cover-slide. As adjacent cells become affected the areas showing these changes increase and spread towards the centre of the preparation. The process may finally affect the entire population of red cells beneath the cover-slide. In duplicate preparations of the same blood sample there is a remarkable similarity in the time of appearance of the changes, the forms produced, and the extent of spread. Dissolution of the spiculated forms

* Sächsisches Serumwerk, Dresden.

1. Shapiro, M. *Congr. int. Transf. Sang*, 1954, p. 365.
2. Caminopetros, J. *Lancet*, 1952, i, 687.

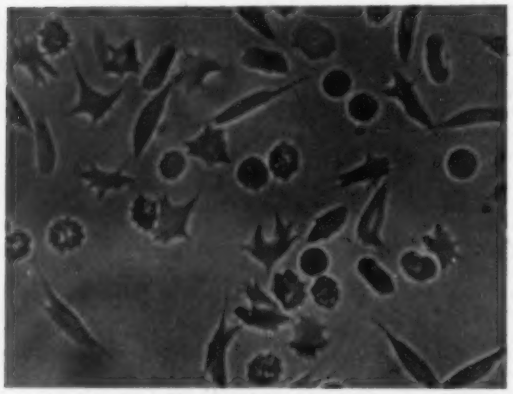


Fig. 2—False sickling: multiple shapes in human cells.

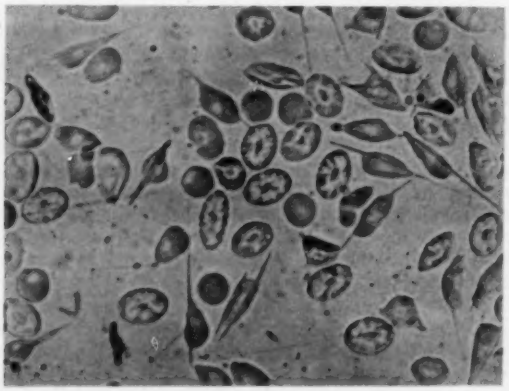


Fig. 3—False sickling in eel's cells.

commences with liquefaction and shrinking of the filaments and consequent involution of the angles of the cells, which then become transformed into glistening prolytic spheres.

Spiculated cells have also been observed in sealed wet specimens prepared from the bloods of cows, pigs, sheep, goats, and other vertebrates. In the nucleated red cells of the eel, *Anguilla mocambica*, filaments of extraordinary length were observed (fig. 3).

The occurrence of the phenomenon in species other than man, the constancy with which the changes can be produced in duplicate preparations of the same blood sample, and the cyclical periodicity observed in human females, all support my hypothesis that spiculated cells represent a true metastable state of the erythrocyte. Berlin [3] has shown that in humans hyperhæmolysis occurs normally in the luteal phase of the menstrual cycle and it may well be that the tendency to spiculation at this time is a related phenomenon.

Failure to recognise these forms as a frequently occurring manifestation in normal human beings of whatever racial origin has undoubtedly been responsible for such fantastically high sickling rates as 46% reported among pygmoids in East Africa,[4] as well as for some erroneous reports of sickling in Greeks [1 2] and Yemenite Jews.[5] That true sickling does in fact occur in Greeks is well known, fig. 1 of Caminopetros' recent paper being a typical example. But it does not follow from this that "false sickling" in Greeks or in any other race of people is an attenuated form of true drepanocytosis.

South African Blood Transfusion Service, Johannesburg. MAURICE SHAPIRO.

LOCAL-AUTHORITY CLINICS

SIR,—I think you are a little unfair to Mr. Richard Cawston in your note about his recent television documentary, *On Call to a Nation* (Oct. 25). You complain that after two general practitioners had roundly condemned local-authority clinics, the contrary arguments were not effectively presented. These clinics are, in the eleventh year of a comprehensive health service, a historical hangover from a previous age. I cannot imagine what arguments in favour of them you had in mind, except perhaps their function as cut-price grocers.

St. Paul's Cray, Orpington, Kent. L. M. FRANKLIN.

*** In 1956 we extracted from The Widdicombe File a letter entitled Clinicosis. Its publication [6] generated a long and vigorous correspondence in which Dr. Franklin will find the arguments we had in mind.—ED. L.

SYRINGE STERILISATION

SIR,—Standard forms of heat indicators should be adopted for all methods of syringe sterilisation by heat. Several different ways of application justify attention and exploration.

The 'Browne Steriliser Control Tube', for example, indicates that certain temperatures have been attained when there is a permanent colour change of a fluid enclosed in a sealed glass ampoule. A suitable permanent colour-change agent might be incorporated in the syringe lubricant smeared on the plunger before closing the syringe prior to heat treatment. An alternative would be for manufacturers of syringes to modify the finger-grip end of the hollow plunger type whereby a replaceable permanent colour-change indicator capillary tube could be inserted inside the plunger. The manufacturer, if provided with a reversible chemical agent selected for its stability, melting-point, and other essential qualities, could place this indicator inside the hollow plunger before final sealing, as a permanent feature of syringe construction. Its position inside the plunger would indicate the heat penetration during sterilisation. These are only a few brief suggestions for direct observation of heat absorption.

The use of such techniques would indicate to everyone using a syringe (irrespective of the form of syringe container, packing or presentation, and information concerning temperature recordings and time exposures) whether in fact sufficient heat had reached the outer surface of the plunger of the closed syringe to assure sterility.

Princess Elizabeth Hospital, Guernsey. HENRY A. WILSON.

CROHN'S DISEASE

SIR,—The conclusion of your leader of Oct. 18 that "perhaps after a quarter of a century, though we know the disease better, we understand it less" is depressing and not quite accurate.

Ten years ago I drew attention [1] to personality factors and the influence of emotional stress in precipitating the onset and relapse of this disease. I have since found that a distinguished American physician [2] and surgeon [3] had already been struck by neurotic traits in these patients. Stewart [4] and Grace [5] confirmed the ætiological importance of emotion and personality in this disorder. Though much remains unexplained about the disease, a reputable textbook of medicine,[6] as long ago as 1954, said this:

> "Though a lack of uniformity of opinion regarding the ætiology of the disease exists, accumulating clinical evidence strongly suggests that it is a psychosomatic disorder. Emotionally, the patients are, and have been, frustrated for one reason or another. Unsatisfactory patient-parent relationships exist. Emotional storms and upheavals precede the onset of the disease and the occurrence of relapses. Most of the patients are very intelligent and are less dependent and more mentally mature than those with ulcerative colitis."

It is surprising, therefore, that you said not a word about all this. Are psychosomatic concepts still so unpalatable that they cannot be mentioned?

I believe the key to understanding the pathology of Crohn's disease lies in its relationship to ulcerative colitis. Firstly, there is the tendency for Crohn's disease to progress after surgery to ulcerative colitis. Secondly, there is the high incidence of both diseases in Jews. Thirdly, sufferers from Crohn's disease have a personality pattern almost indistinguishable from that now increasingly accepted as specific in ulcerative colitis; and fourthly, similar forms of stress are especially provocative in both disorders. It is, therefore, a reasonable assumption that the initiating factor is persistent or recurrent acute ileitis due to excessive motor activity and vascularity (possibly parasympathetically mediated) and to emotional stress. The ileocæcal area, rich in lymphatics and lymphoid tissue, may be especially prone to lymphœdema when lymphatic drainage is impaired as a result of chronic inflammation. This lymphœdema was described by Hadfield [7] as the essential early manifestation of the disease.

The objection to this hypothesis is that patients with ulcerative colitis do not get Crohn's granulomas in their colons very often. The colon *can* produce the typical Crohn's lesion; indeed the whole gut can be affected (though it is probably relevant to the lymphatic-drainage hypothesis that the lesions elsewhere are not so massive as those in the ileocæcal area). If the disease were limited to the ileocæcal region it would be just possible to explain the difference between colitis and Crohn's disease on the basis of the anatomical distribution of the lymphoid tissue alone, but it is not possible, and there must be another factor. I suggest that this is an excessive or abnormal host response of the lymphatic system to non-specific

3. Berlin, R. *J. clin. Path.* 1951, **3**, 286.
4. Lehmann, H., Raper, A. B. *Nature, Lond.* 1949, **164**, 494.
5. Dreyfuss, F., Mundel, C., Benyesch, M. *Harefuah*, 1951, **41**, 168.
6. *Lancet*, 1956, ii, 781.

1. Paulley, J. W. *Lancet*, 1948, i, 923.
2. Bockus, H. L. *J. Amer. med. Ass.* 1945, **127**, 449.
3. Cave, H. C. *ibid.* p. 205.
4. Stewart, W. A. *N.Y. St. J. Med.* 1949, **49**, 2820.
5. Grace, W. J. *Gastroenterology*, 1943, **23**, 542.
6. Harrison, T. R. Principles of Internal Medicine; p. 1564. London, 1954.
7. Hadfield, G. *Lancet*, 1939, ii, 773.

chronic gut inflammation, and that a parallel may be found in sarcoidosis, which is thought sometimes, if not always, to present as an abnormal reticuloendothelial response to the tubercle bacillus. A specific organism, such as a virus or even the tubercle bacillus, is obviously not excluded, but if it exists, the psychosomatic observations all point to its entry into the gut wall as being secondary.

These patients share with colitis sufferers their sensitivity, some of their immaturity, and also an incapacity to tolerate strife, argument, harsh words directed at them or in their environment. Whereas colitis patients walk away from a quarrel and brood, those with Crohn's disease are often peacemakers, and try to pour oil on troubled waters. They are thought of by many as "very nice people".[8] They tend to have rather more to say for themselves than ulcerative-colitis subjects, and are sometimes less demanding and querulous. They are more readily accepted in a group, such as a ward, where subterfuge is often needed to prevent the flat rejection of the colitic by other patients.

It should be clear, therefore, that in Crohn's disease it is not enough for the surgeon to operate and return the patient to his old environment. Some attempt should always be made to explore and understand the psychosomatic aspects of the disease. If psychotherapy is started postoperatively, relapses may be reduced; if it is started preoperatively, surgery might at times be avoided altogether, especially with the aid of steroids.

Ipswich. J. W. PAULLEY.

"INCIDENCE" OF HYALINE MEMBRANE IN PREMATURE INFANTS

SIR,—The Silvermans' letter of Sept. 13 makes an important point regarding the "incidence" of hyaline-membrane disease. They determined the "incidence" of fatal cases by using the numbers dying over numbers born in each weight group. The results of this calculation suggest that the disease is more common the more premature the infant. A preliminary review of the experience at Boston Lying-in Hospital confirms this trend.

The emphasis in the Silvermans' letter was on the choice of an appropriate denominator. Although they note the difficulties with regard to the numerator, we feel this part of the calculation deserves further comment. The ratio of fatal cases to live births (the Silvermans' "incidence" rate) is in fact a measure of mortality. The relationship between the two is expressed by the formula: mortality = incidence × case-fatality, where the case-fatality, defined as deaths over cases, is a measure of the risk of death from the disease once it has been contracted. As the Silvermans point out, an important assumption in their calculation is that the risk of death from the disease is the same regardless of birth-weight. We have no way of examining this assumption directly. Perhaps the predisposition of smaller infants to pulmonary infections, intracranial hæmorrhage, &c., means that some with the disease die who would have survived in the absence of complications. Until we have a way of establishing the diagnosis ante mortem we cannot answer the question of incidence with certainty.

With many factors in the background which singly or in combination may predispose to death from the disease, conclusions depending on only one of these are open to question. For instance, as the Silvermans note, the frequently quoted association of cæsarean section and hyaline-membrane disease may be an example of isolating a possible predisposing factor and disregarding others, such as prematurity and maternal diabetes.

Newborn Service, Boston Lying-in Hospital. MARY ELLEN AVERY.
Department of Biostatistics, Harvard School of Public Health. MARGARET DROLETTE.

8. Meeting of Society for Psychosomatic Research, London, Oct. 16, 1958.

OCULAR LESIONS OF ONCHOCERCIASIS

SIR,—We have read with some concern Mr. Choyce's recent contribution[1] and your annotation[2] on this subject.

At a recent meeting of ophthalmologists we were agreed that there is overwhelming epidemiological evidence in favour of the view that onchocercal infection is directly responsible for the blinding lesions of the fundus, iris, and cornea, which have in the past been attributed to onchocerciasis. Moreover, in surveys which we conducted together in the French Sudan we demonstrated the high incidence of these lesions in two onchocercal villages and their complete absence in a non-onchocercal village in the same area. These conclusions will be published.

Your statement that the fundus lesion does not appear to have been observed in Central and South America is incorrect.[3–5] We would stress that lesions resembling familial choroidal sclerosis in appearance may well be environmental in ætiology.[6] A detailed criticism of the symposium on onchocerciasis held by the Royal Society of Tropical Medicine and Hygiene is in press.[7]

We hope that enthusiasm for Mr. Choyce's "exciting development" will not overshadow the previously published evidence, from almost every country where onchocerciasis has been reported, pointing to the causal relationship between onchocerciasis and blindness.

ROGER R. D'HAUSSEY
Formerly Director
G. LE BRETTON OLIVEAU
Director
L'Institut d'Ophtalmologie de l'Afrique Occidentale Française, Bamako, French Sudan.
Luluabourg, Belgian Congo. MICHEL AUBRY.
Paris. ALBERT VANDENDORPE.
Kaduna, Nigeria. JEAN LAGRAULET.
Nairobi, Kenya. F. H. BUDDEN.
Accra, Ghana. G. G. BISLEY.
C. O. QUARCOOPOME.

SHORTAGE OF JUNIOR HOSPITAL STAFF

SIR,—The points raised in this correspondence are important in principle but they must also affect directly numerous individuals. It is frightening to see recourse to compulsion being advocated (Mr. Henderson, Oct. 18) when we are already effectively hedged on every side by restrictions. The attempts to enumerate the causes of staff shortage in small hospitals, and the suggestions for removing them, make this an important topic for discussion.

Once experience has been gained on the spot we are able to bring added wisdom to the, by then, academic question of whether we should, or should not, apply for a preregistration post at the periphery. Dr. Manson (Oct. 25) takes a typically wise retrospective view from such a vantage point of wide experience.

I wonder if the factors pro and con which have come to light in this correspondence are, in fact, in the mind of the new graduate when he decides that he will make every effort to avoid going to a peripheral hospital. It is more likely that he has not the necessary knowledge on which to base an opinion and he makes his decision either on the direct advice of his more senior colleagues, or on the implied advice gained over the years as a student.

Is it possible that our teachers are not aware of the high standard of work often (perhaps usually) practised in small

1. Choyce, D. P. *Trans. R. Soc. trop. med. Hyg.* 1958, **52**, 95.
2. *Lancet*, 1958, i, 1165.
3. Quevedo, A. *Amer. J. Ophthal.* 1941, **24**, 1185.
4. Clark, W. B. *Trans. Amer. ophthal. Soc.* 1947, **45**, 461.
5. Lagraulet, J. *Mém. Soc. française Ophtal.* (in the press).
6. Sorsby, A., Mason, M. F. J., Gardener, N. *Brit. J. Ophthal.* 1949, **33**, 90.
7. Budden, F. H. *Trans. R. Soc. trop. Med. Hyg.* (in the press).

hospitals now that facilities once peculiar to the centres of medical education are more generally available? If the attitude to the small hospitals as a suitable training ground for new graduates becomes more in keeping with the work carried on in them our reluctance on graduating might well change to eager competition for preregistration posts at the periphery.

Chester City Hospital, Chester. E. S. WILLIAMS.

ABSORPTION OF BOUND RADIOACTIVE VITAMIN B_{12}

SIR,—I fully agree with Dr. Nyberg and Dr. Reizenstein (Oct. 18, p. 832) that real information with regard to the mode of action of intrinsic factor will come only from the study of the absorption of vitamin B_{12} bound to protein. It has perhaps been unfortunate in the past that workers in this field have for the most part studied absorption after administration of the vitamin in the free form.

It is interesting that Dr. Nyberg and Dr. Reizenstein have demonstrated the existence in pig liver of a vitamin-B_{12} binder which is capable of bringing about intestinal absorption of the vitamin in patients with pernicious anæmia. It is important, however, to note that the protein-vitamin complex obtained from pig liver is apparently susceptible to the action of chymotrypsin and trypsin and would, therefore, be broken down in the intestine.

In my own laboratory, absorption studies have been carried out with a combination of sow's milk protein and vitamin B_{12}. Only a small amount of the vitamin becomes ultrafiltrable after treatment with trypsin.[1] Moreover, the mode of combination with the vitamin is similar to that occurring in intrinsic-factor preparations.[2] I have already pointed out [2] that it is possible that binding by the latter is due to the presence of impurity and that vitamin B_{12} bound to this is absorbed in the presence of intrinsic factor. My own recent observations have now shown that when 0·5 μg. of radioactive vitamin B_{12}, in the form of a complex with sow's milk protein, is administered to patients with pernicious anæmia there is no demonstrable absorption. This contrasts with the fact that not infrequently there is appreciable absorption when this amount of the vitamin is given orally in the free form. It has been equally striking to note that when the same amount of sow's milk/vitamin-B_{12} complex was given to patients with pernicious anæmia along with an intrinsic-factor preparation approximately 0·3 μg. of the vitamin was absorbed. This seems to indicate, as we would expect, that the function of intrinsic factor is to make available for absorption dietary vitamin B_{12} originally in the bound form. Whether it does this by some form of proteolysis or whether it brings about the transfer of the vitamin to some absorbable binder is not yet known.

We have also studied the binding substance present in bile and have demonstrated that, although some of the vitamin B_{12} bound by human bile is absorbed by normal rats, the absorption is definitely less effective than when the vitamin is given alone.

It is hoped shortly to publish these experiments in greater detail.

Dr. Nyberg and Dr. Reizenstein refer to the "B_{12}-peptide" of Heathcote and Mooney.[4] I feel I ought to point out that I now have much chemical evidence which indicates that their preparation is not a vitamin-B_{12}-peptide but a mixture of free vitamin B_{12} with some peptide and some protein. It is possible that the mild extraction procedures which have been used for obtaining material from the commercial preparation may possibly have split a vitamin B_{12}-peptide. If this is the case, however, there can be little doubt that similar splitting would occur in the intestine and the mechanism of absorption would in effect be the same as if free vitamin B_{12} had been administered.

I wish to thank Dr. E. S. Holdsworth for the sow's milk protein material.

Department of Pathology,
King's College, University of Durham,
in the Royal Victoria Infirmary,
Newcastle-upon-Tyne. A. L. LATNER.

SIR,—In their preliminary communication Dr. Nyberg and Dr. Reizenstein demonstrated that radio-vitamin B_{12} stored in pig liver is absorbed with remarkable ease by normal subjects and patients with pernicious anæmia. This interesting finding offers a good explanation of why oral liver was successful in the hands of the early students of pernicious anæmia. However, as shown by the data we give below, totally gastrectomised rats are unable to utilise radiovitamin B_{12} contained in rat liver.

Normal rats were given an injection of 100 mμg. (=100 mμc.) ^{60}Co-labelled vitamin B_{12} daily for 2–3 weeks and were killed by decapitation 3 days after the last injection. The livers were stored frozen until used. Microbiological assay with *Euglena gracilis* indicated that the livers contained approximately 140 mμg. vitamin B_{12} per g. Two series of experiments were performed: in the first series a saline homogenate (1 ml.=100 mg. liver), in the second whole pieces of liver (weighing about 100 mg.) were administered. In the first series the normal rats excreted on the average 35% (range 31–40) of the oral radioactivity, whereas the totally gastrectomised rats excreted all of it (mean 102%, range 98–103). Findings were similar in the series in which pieces of liver were fed.

These experiments demonstrate that the hepatic radioactivity behaves like cyanocobalamin when rat liver is fed to gastrectomised rats. In our experiments the oral dose corresponded to about 14 mμg. of vitamin B_{12}, which is still in the range where the presence of intrinsic factor has a profound influence on the absorption.[1] On the other hand, the dose of pig liver used in the experiments of Dr. Nyberg and Dr. Reizenstein was relatively high. Thus the absorption may have been facilitated by increased diffusion and/or the presence of concomitant substances with a sorbitol-like action, rather than by an "activated" vitamin-B_{12} compound. The difference in species may also have played a part.

Department of Medical Chemistry,
Helsingfors University, Finland. RALPH GRÄSBECK.
LARS RUNEBERG
KAI SIMONS
Central Hospital, Vasa, Finland. WOLMAR NYBERG.

TREATMENT OF GONORRHŒA

SIR,—It is not only in London that penicillin-resistant gonorrhœa has been encountered (as described in your annotation of Oct. 11), for the same phenomenon has now been seen in Liverpool. In May of this year it was decided to revert to the practice, discontinued in 1953, of treating men with gonorrhœa with single injections of 300,000 units of penicillin in oily suspension with 2% aluminium monostearate (P.A.M.) Of 46 cases so treated, 7 failed to respond and gonococci persisted in their urethral discharge following treatment. The series is admittedly small but is, we feel, significant when compared with a report from the same centre some years earlier when no failures were reported in a rather larger series of cases.[2]

In any attempt to interpret these results it should be pointed out that, whereas prior to last May no penicillin

1. Gregory, M. E., Holdsworth, E. S. *Biochem. J.* 1955, **59**, 335.
2. Gräsbeck, R. *Acta. chem. scand.* 1958, **12**, 142.
3. Latner, A. L. *Lancet*, 1958, i, 1077.
4. Heathcote, I. G., Mooney, F. S. *ibid.* p. 982.

1. Clayton, C. G., Latner, A. L., Schofield, B. *Brit. J. Nutr.* 1957, **11**, 339.
2. Alergant, C. D. *Brit. J. vener. Dis.* 1953, **29**, 34.

had been used for five years in the treatment of gonorrhœa in males, penicillin had continued to be the routine treatment for all female patients suffering from gonorrhœa. You may not have been aware of this practice which, in retrospect, seems to have had unfortunate results.

Liverpool Royal Infirmary. C. D. ALERGANT.

SEVERE HEAD INJURIES

SIR,—I should like to congratulate Mr. Maciver and his colleagues on their excellent articles,[1 2] which should be read by every surgeon and casualty officer and by those in charge of the ambulance service. The problems involved were lucidly brought to the notice of anæsthetists by the Oxford School as long ago as 1950.[3]

In dealing with these cases I should like to emphasise:

(*a*) The importance of passing a large stomach tube at the earliest possible moment after the injury.

(*b*) The need to watch for pulmonary œdema of central origin which may develop suddenly and rapidly prove fatal. This may be associated with Cheyne-Stokes respiration and pyrexia. These should be dealt with by an intensification of the dehydration therapy, positive-pressure respiration with an appropriate machine connected to the tracheotomy tube, and cooling.

(*c*) The crying need for an intensive therapy unit at every major hospital. These units should be fully equipped and staffed by senior nurses throughout the 24 hours. Only in this way will the unconscious patient, no matter what the cause of the unconsciousness, receive the treatment he has a right to expect and which the more recent advances in therapy can offer. Finance and cold surgical and medical waiting-lists should not be permitted to stand in the way of setting beds aside for this urgent need of humanity and progress.

Hull. W. N. ROLLASON.

HOSPITAL BEDDING

SIR,—Your readers may like to know that the disinfection process referred to by Dr. Caplan at the meeting of the Association of Clinical Pathologists (*Lancet*, Oct. 18, p. 833) is in use at Highlands General Hospital, Winchmore Hill, London, N.21.

The cost of converting the autoclave was £150, the apparatus being supplied by Messrs. Manlove Alliott & Co. Ltd.

Hospitals with large stocks of woollen blankets, which they do not wish to discard immediately, may find this an economic method of preventing cross-infection whilst changing over to cotton blankets. Even when the change has been made, this process will be an additional safeguard, especially in the case of hospitals which have to send their laundry to outside contractors and therefore have no control over the washing process.

Northern Group Hospital Management Committee, London, N.7. A. F. GRAY Secretary.

SIR,—I refer to the interesting article by Dr. Schwabacher and her colleagues (Oct. 4), and I would congratulate them on the thoroughness and scientific methodology of their trial.

I would, however, also draw attention to a distinct mis-statement in your annotation—that "there is still no method other than autoclaving for disinfecting mattresses". In fact, Sparkhall Vapour-Gas Disinfectors have been used for many years extensively in British and overseas hospitals, being specially designed for disinfecting mattresses of all kinds, as well as blankets, bedding, clothing, and toys made by occupational-therapy patients.

Because mattresses vary so much in size, almost from one hospital to another, the Sparkhall Company actually makes the racking of its disinfectors literally "to measure" for individual hospitals in order to ensure maximal efficiency through optimal circulation of the disinfecting medium, which is an important feature, as is the case with all other disinfecting methods, including high-pressure steam plus vacuum.

Because damage to the fabric of mattresses and blankets is a constant and expensive consideration, the fact that neither shrinkage nor other damage can result from the use of the Sparkhall system is an important advantage.

Sparkhall Steriliser Co., Ltd., West Croydon, Surrey. D. F. J. HEXT-FREMLIN Managing Director.

CARCINOMA OF THE CERVIX

SIR,—The article you published last week on cervical smears as a means of detecting presymptomatic carcinoma of the cervix was a model of reporting which all contributors to medical journals would do well to emulate. The investigation was simple, and the presentation concise and easily understood.

He who is interested in maintaining the highest standards in general practice must ask the following questions:

Since the discovery-rate of carcinoma of the cervix was about 1·5% to 2·0%, and the team suggested that this technique was one which might reasonably be adopted in general practice, do the individual members of the team intend to pursue this routine as a regular part of their daily work? If so, how often? Will they take smears every year from every woman between say 30 and 60 years of age?

Assuming that about half of these women with presymptomatic carcinoma of the cervix would have been cured if and when they presented as clinical cases, do the team still intend to adopt the routine in their own practices?

Bearing in mind that routine electrocardiography will reveal an unknown number of cases of coronary heart-disease, that routine testing of urine will reveal about 2% of unsuspected and unsuspecting diabetics, and that the taking of routine hæmoglobins will reveal a host of unknown anæmic women, does the team seriously suggest that general practitioners should embark on these projects as a routine?

These are questions that we have to face; for on every side we are subjected to a torrent of advice as to how we are to use the new techniques of our trade. It is a good thing that investigations such as that into carcinoma of the cervix should be carried out, but it is another to suggest that such techniques should be adopted as routine. Any doctor who is interested in the presymptomatic detection of disease looks like having his life materially shortened by overwork.

Darbishire House Health Centre, 295, Upper Brook Street, Manchester, 13. H. W. ASHWORTH.

SIR,—In your issue of Oct. 25 there is a leading article about cancer of the cervix, and a report on the elaborate and careful cytological screening of 1000 women.

May I say that if practitioners and gynæcologists, in all cases where they find abnormal cells in the vagina or in the cervix, would be wise enough to give thyroid by mouth at once or, failing that, thyroid in an ointment base, locally, they would see how these abnormal cells disappear after 3–4 weeks of treatment—especially if gr. 3 of thyroid daily is given by mouth. The thyroid hormone changes completely the enzymatic happenings in the cells and the so-called cancer-in-situ cells disappear.

I would not go so far as to say that already invasive processes can be abolished, but as I described in my earlier works,[1 2] thyroid hormone given in bigger doses

1. Maciver, I. N., Frew, I. J. C., Matheson, J. G. *Lancet*, 1958, i, 390.
2. Maciver, I. N., Lassman, L. P., Thomson, C. W., McLeod, I. *ibid.* Sept. 13, 1958, p. 544.
3. Bryce-Smith, R. *Brit. med. J.* 1950, ii, 322.

1. *Brit. med. J.* 1954, ii, 1380.
2. *J. internat. Coll. Surg.* March, 1958.

reinforces the body cells against cancer-cell formation via histamine production—regarded today as a hormone.

I would especially advise the radiotherapists to use thyroid hormone, as deep X rays in any form rob the tissue of histamine and that is why everyone who uses McWhirter's therapy should think of this.

London, W.1. A. A. LOESER.

INTRA-ARTICULAR THERAPY IN RHEUMATOID ARTHRITIS

SIR,—The article by Dr. Chandler and his colleagues (Sept. 27) contains examples of unsound statistical thinking. My complaints are these:

(1) If the odd device of plotting 't' against time is used the reader is entitled to see the figures from which 't' is calculated.

(2) It seems that 't' was calculated from arbitrary categories and not from measurements. It is doubtful if Gosset's 't' test is applicable in these circumstances.

(3) "Probably significant improvement lasted eight weeks." What does this mean? Statistical significance is a phrase statisticians use to tell non-statisticians what they mean by P. To say that something is probably significant is nonsense.

(4) "It is possible, but unlikely, that larger numbers might show . . ." There can be no excuse for such a conclusion. In the material published there is no evidence of what the result might have been if an experiment had been done.

If the relative potencies of two effective drugs are to be compared and there is not much difference between them, then either a more sensitive method of measuring effect must be devised or the numbers entering the trial must be increased. The authors have not answered the question they asked.

London, S.E.3. GEOFFREY E. LOXTON.

BANTING UP TO DATE

SIR,—Darwin did not originally advance his theory to explain the adaptation of all living organisms solely to their "natural" environment. He described variation under domestication at greater length in *The Origin of Species* than variation in nature. In 1868 he completed *The Variation of Animals and Plants under Domestication.*

He had a certain amount to write about diet. He pointed out how marvellously varieties could become adapted to diets, which varied remarkably from those of their ancestors, and he gave it as his opinion that an excess of food made for variation.

A natural environment or natural diet has no meaning, as applied to *Homo sapiens.* We live in houses, wear clothes, walk in shoes, eat cooked food, and are educated by more than experience. Is it natural to use a fountain pen or should it be a quill? Our milk is cow's milk and such uncooked foods as we eat are nearly always of highly domesticated varieties. Our natural functions are better performed in a civilised way.

The natural man, who can still be found, in diminishing numbers, does not present an encouraging contrast. Natural selection is eliminating him. If he does not suffer from obesity it is probably because he is diseased and has nothing much to eat. Concentrated carbohydrates may be responsible for obesity but all our food is more or less unnatural.

Naturalism is a false god. Taoism, Stoicism, and Epicureanism and attractive religious philosophies containing the seeds of their own decay. Science is observation and the answers to medical problems are not to be found in metaphysics.

Catterick, Yorks. D. HAMILTON.

Obituary

JOHN WALLACE DICK MEGAW

K.C.I.E., Hon. D.Sc. Belf., M.B. R.U.I.

A FORMER director-general of the Indian Medical Service, Sir John Megaw died on Oct. 24, in his 85th year. His pioneer work on tropical diseases, much of it in association with Sir Leonard Rogers, has long been famous.

John Wallace Dick Megaw was born in 1874, the son of John Megaw of Ballyboyland, County Antrim. He was educated in Belfast, taking the B.A. of Queen's College in 1895 and the M.B. in 1898. He entered the Indian Medical Service by competition in 1900 and went over to the civil side of the service in 1903, when he was posted for duty in Bengal. As a district medical officer, he rapidly showed his all-round competence, but he soon developed a special interest in problems of hygiene, pathology, and bacteriology. He took up resident duty at the Medical College Hospital in Calcutta, and there began his long association with Leonard Rogers when they together studied the effects of hypertonic intravenous saline in cholera.

When the new province of Bihar and Orissa was carved out of Bengal, Megaw's duties took him there for a time, but his postgraduate studies in Europe determined his future, and in 1914 he was appointed professor of pathology in Lucknow University, a post which he subsequently combined with that of principal of the Medical College. As a teacher and organiser of museums and as a medical research-worker Megaw made his mark at Lucknow. His principal researches were concerned with beriberi, epidemic dropsy, and the short fevers of India (dengue and sandfly fever). While on holiday in the Kumaon Hills he was bitten by a small arthropod, and a feverish illness and petechial rash developed. This historic illness was recorded by Megaw as tick typhus, and although he probably in fact had mite typhus, this was the starting-point of modern work in Asia on endemic rickettsioses.

When, as the result of Sir Leonard Rogers' drive and his appeals to the merchant princes of Calcutta, the Calcutta School of Tropical Medicine with its associated hospital was finally completed, Megaw was chosen as director and professor of tropical medicine. He gathered a strong research team, including Acton, Knowles, Lloyd, Chopra, Napier, and Pasricha, and in a short time he raised the prestige of the school to a very high level with a steady output of research from all the departments.

Megaw was particularly interested in the effects of heat and humidity on working capacity. His office in Calcutta (and later offices in Madras and Delhi) were fitted with window screens of khus-khus branches and twigs kept moist by dripping water, through which an electric fan played. His efforts encouraged others to try to maintain working efficiency throughout the heat of the Indian day.

In addition to his administration, teaching, and research Megaw edited the *Indian Medical Gazette* from 1921 to 1929. In 1928 he went to the Punjab as inspector-general of hospitals, but a few months later he was promoted major-general and held the appointment of surgeon-general with the Government of Madras. It was in 1930 that he became director-general of the Indian Medical Service; and he was appointed a knight commander of the Indian Empire in 1933. He held the post of honorary physician to the King from 1930 to 1933. His university conferred on him an honorary D.SC. in 1934.

When he retired from the I.M.S. in November, 1933, he succeeded Sir Leonard Rogers as medical adviser to the Secretary of State for India in London. At the same time he held a part-time lectureship at the London School of Hygiene

and Tropical Medicine, where he was concerned specially with the rickettsial diseases and other subjects on which he was an authority. He retired from the India Office in 1939.

Of Sir John's work in India and his characteristically vigorous years of retirement, G. R. McR. writes:

"With the death of Sir John Megaw the almost legendary link between him and Sir Leonard Rogers has been broken and many will mourn in Asia. In India Megaw was regarded as a medical statesman. With his background as district medical officer, research-worker, teacher, and provincial administrator he made the ideal director-general. He heartily disliked pomp and protocol and could never be induced to be photographed in full-dress uniform. Fully sympathising with constitutional advance in India he constantly emphasised the urgent need to train our Indian successors. For many years he devoted much of his abundant energy to publicising the evils of excessive birth-rates and of overpopulation. He was a powerful advocate of instruction in the technique of control of conception, years before it became the official policy of the Government of India.

"During his retirement he took up farming in earnest to 'grow more food'. On his small estate in Kent, he worked like a Trojan. He was always much younger than his years both in appearance and habits; and until just before his death he was active all day long as a practical farmer, driving his tractor and his Land Rover over the roughest ground like a man half his age.

"As a sectional editor of the *Tropical Diseases Bulletin* Megaw was one of the most conscientious, accurate, and prompt contributors. Till 1957, when he asked permission to make room for a younger man, he scanned the medical press of the world for new work on plague and rickettsioses, which were his abiding interest. His chief hobby was working on a new international language which he hoped would be an improvement on existing systems."

P. M.-B. also speaks of Sir John's influence in India and of the way he profitably applied his wide experience after his retirement:

"The name of John Megaw stands high in medical India, where he played a big part in medical education. A lifelong friend of Sir Leonard Rogers, he won a worldwide reputation as coeditor of their book, *Tropical Medicine*, which is still regarded as the standard work on this subject as applied to India. After his retirement, he acquired new lustre as sectional editor of the *Tropical Diseases Bulletin* concerned with the difficult and intricate typhus group. He had acquired such a wide knowledge of the rickettsioses that not only was he able to review the world literature with an authority seldom equalled, but also, with uncanny perspicacity, to inspire new avenues of research. He thus performed a great and welcome service."

In 1912 Sir John married Helen Esmée Ward, who survives him.

DALZIEL BUCHANAN McGRIGOR

O.B.E., M.B. Aberd., F.A.C.R., D.M.R.E.

Brigadier D. B. McGrigor, a former president of the British Institute of Radiology and consultant in radiology to the Army, died on Oct. 22 at the age of 73.

Born at Torry, Aberdeen, the son of a consulting engineer, he was educated at Robert Gordon's College, Aberdeen, and graduated from Aberdeen University in 1907. He joined the R.A.M.C. that year and served in India from 1909 to 1914. He returned to active service in France with the Indian Expeditionary Force and was in charge of a field X-ray section. In 1918 he was again in India as D.A.D.M.S., 9th Indian Division, and specialist in electrical services. In 1920 he was appointed specialist in charge of radiology at Queen Alexandra Hospital, Millbank, and lecturer in the R.A.M. College. He retired from the active list in 1927.

From 1924 to 1939 he was on the committee of the British Institute of Radiology; in 1939 he was the institute's treasurer, and from 1939 to 1942 its president. In 1939 he was recalled from the Reserve as adviser in radiology, and he organised the Army School of Radiology. He was promoted brigadier in 1941 and his duties took him on tours of inspection to North Africa, the Middle East, and later France. From 1945 until his retirement in 1952 he was honorary consultant and examiner in radiology to the Army.

He was appointed O.B.E. in 1919 and his other distinctions included the honorary fellowships of the American College of Radiology and the Society of Radiographers.

In addition to his substantial contributions to military radiology, which included work on stereoscopy and the invention of a localiser for foreign bodies in the eye, Brigadier McGrigor was also devoted to his duties as secretary of the R.A.M.C. Officers' Widows and Orphans Friendly Society. As H. J. B. recalls "he was an ideal secretary, with a particular flair for the work involved, and took tremendous pains in his record-keeping and the collection of financial advice for the guidance of the committee of management. It is difficult to think of the 'Widows and Orphans' without McGrigor."

"I always associate McGrigor with the hearthrug in front of the west fireplace of the smoking-room of the Millbank Mess, where I first met him in the early 1920s. It was just before lunch and he was standing with a group of friends telling some story, while Elliott, the old wine steward, was ministering to their needs. That picture was to be repeated again and again: McGrigor standing and some of the others sitting on the broad fender rail of the fireplace. It was always a very friendly group, each contributing to the talk; but McGrigor was the central figure, not merely because he was a big man and stood well, and certainly not because there was any aggression about this dominance: it was just strength of personality. I never heard him addressed or referred to as anything other than 'McGrigor' by his colleagues; but this had nothing to do with seniority or approachability: nobody was a better mixer, easier to talk to, more courteous to strangers, or kinder to those who sought his help or advice.

"McGrigor rarely talked shop in the Mess and it was not until the late war, when he was consultant radiologist to the Army, that I came to appreciate his great ability and experience in this field and the respect he commanded in his dealings with his fellow radiologists. He was an excellent organiser and ran his department with a minimum of fuss and bother, yet he did so much."

At the outbreak of war in 1939 radiological equipment for the Army had to be produced very quickly and McGrigor's efforts achieved remarkable results. But perhaps his greatest contribution to Army radiology, W. F. M. suggests, was "his flair in selecting the right man for the job."

"Several radiologists who were serving with line regiments were (albeit sometimes reluctantly) extracted by him to serve in their specialist capacity, and within a relatively short time he had built up a team of men who were thereafter referred to as his 'boys' (irrespective of their age).

"Tall and genial, he loved meeting people and talking to them. Perhaps he was never so happy (apart from when he was mending old clocks) as when, touring the length of the land, he took pains to call on his former officers, and his pleasure at meeting them again was matched by their pride in welcoming their old chief. He paid several visits to the United States at the invitation of American radiological societies, and his lectures, interspersed with pawky Scottish anecdote, were acclaimed both for their professional content and their humour. His services to the radiological branch of the American Forces were recognised by the award of the Legion of Merit.

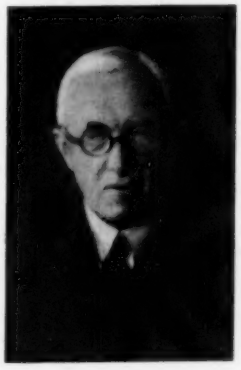
"By his death the Army has lost its doyen of radiologists, and all those who were privileged to serve under him will long mourn the passing of a great-hearted and faithful friend."

He married in 1912 Dorothy Macgregor Drysdale, who survives him with two sons, both doctors, and a daughter.

JAMES ANDREW GUNN

C.B.E., M.A., M.D., D.Sc. Edin., D.M. Oxon., F.R.C.P.

Prof. J. A. Gunn, who died in Oxford on Oct. 21, took up the study of pharmacology at a time when the science was growing rapidly, and he turned to brilliant advantage the opportunities it offered. By his vigorous research and teaching at Oxford and his years of strenuous work for the Pharmacopœia Commission he made outstanding contributions both to pharmacology and to medicine as a whole.



Elliott and Fry

He was born in Kirkwall 76 years ago and never lost his gentle Orcadian accent. At Edinburgh he took the degrees of M.A., B.SC., M.B., CH.B., M.D., and D.SC. before he was 28, winning many high distinctions in the process. He was appointed assistant in the department of materia medica under the famous Sir Thomas Fraser, who had done so much to lay the foundations of the scientific study of drugs in Britain, but was now an old man, busy with clinical practice and important public duties. A heavy load of teaching fell on Gunn, but he started experiments on a variety of subjects at a time when the professor was unable to give him real help or encouragement. He published papers on the fly-catching reflex produced in frogs by yohimbine, on the action of arsenic on the blood, and on cobra venom. He was awarded a Beit fellowship in 1912, with the distinction of official authorisation to work on four different problems; but before he could do so he was appointed reader in pharmacology at Oxford. There had previously been no pharmacological department at Oxford, but Gunn quickly started a practical class and a popular course of lectures. He was active in research and encouraged a number of younger men to become pharmacologists. He was made professor of pharmacology in 1917, and held this post until 1937, when he was succeeded by Prof. J. H. Burn. From 1937 to 1946 he was professor of therapeutics in Oxford and lived in the old Radcliffe Observatory, which had been converted into the Nuffield Institute of Medical Research.

During Gunn's life pharmacology rose from obscure beginnings to be an important science and an important part of the medical curriculum; and he played an active part in these changes. It was at his suggestion that the British Pharmacological Society was started in 1931 by a group of about twenty pharmacologists, who met in Wadham College the day before a meeting of the Physiological Society. He presided over the business meeting when the society was formed, and the first scientific meeting was held in his laboratory.

He was chairman of the British Pharmacopœia Revision Committee from 1939 to 1948 and was thus responsible for this work during the war and for the important *Pharmacopœia* which appeared in 1948.

One of his major scientific interests was the alkaloid harmine and its various derivatives. His first paper on this subject was written in 1909, and he reviewed the whole subject in an article published in 1937. These alkaloids stimulate the uterus and relax the intestine, but their interest depends mainly on their actions on the central nervous system where they may cause hallucinations and dreams. There has been much discussion in recent years of these actions, which are thought by some to depend on the presence of an indole nucleus in the structure of these and other alkaloids.

He was also interested in symptahomimetic amines, and his views were summarised in the Oliver-Sharpey lectures which he delivered before the Royal College of Physicians of London in 1939. He obtained particularly interesting results with methoxy compounds, which had a strong central stimulant action, and whose effects on small muscle depended on the species of animal used.

Professor Gunn edited the 12th edition of Cushny's *Textbook of Pharmacology and Therapeutics*. His own *Introduction to Pharmacology and Therapeutics*, which first appeared in 1929, was popular because it said all that was really essential in simple language. It was intended for students to read before they attended lectures, and it was so successful that new editions appeared at short intervals (the 9th appeared this year).

Of his prodigious efforts as chairman of the Pharmacopœia Commission, D. H. writes:

"On the death of A. P. Beddard, Gunn became chairman of the Commission in November, 1939. A new *Pharmacopœia* was due to be published in 1941, and, although at the outbreak of war it was well on its way to completion, we realised that to attempt a complete new issue would be impracticable. During the war, in order to secure the inclusion of substances and preparations which advances in knowledge had shown to be desirable additions, and also to provide substitutes for, or alternatives to, substances which under war conditions had become unprocurable or were hard to get, six further addenda to the 1932 *Pharmacopœia* were issued.

"Ably helped by Dr. C. H. Hampshire, secretary of the Commission, Gunn worked at full pressure. His sedulous care for the maintenance of his own standard of work in the six addenda and in the *B.P.* of 1948 involved the serious strain of travel in war conditions and all the difficulties arising from destruction by bombing and fire of our records in the G.M.C. building. The need for copious revisions and alterations arose principally because of shipping difficulties. We could not get aloes from Socotra because the ships were needed for aeroplanes. And in many ships sunk by torpedo were badly needed galenicals.

"Gunn was throughout kind, courteous, considerate, and witty. His features were rugged and rough-hewn. The streptococcal septicæmia which had attacked him in 1917 led to cavernous-sinus thrombosis, leaving him with a blind eye. Somehow this made his smile and his chuckle all the more charming, as at one meeting when he said, 'What shall we do about Grindelia? It's a nauseous preparation sometimes given for asthma. I think it would be a good name for a girl.' His sense of fun sometimes led him into the attack. On one occasion we were considering gelsemium, which is the dried root of American yellow jasmine. H. was adamant that tr. gelsem. B.P.C. (m. v to xv) is worthless as used for migraine and neuralgia. When Gunn summed up by saying, 'The neurologists want gelsemium put back in the *Pharmacopœia*; we ought to educate them above this,' the meeting threw it out.

"He always put us at our ease in difficult circumstances. Each one of us had his loyal backing if we did stupid things. For example, I was chairman of the vitamin committee and in those days biological standardisation was not fully grasped by the ordinary routine pharmacist, but Gunn gave me a free hand to coopt anybody I wanted in Great Britain. I had to confess to him that often I could not understand what they were saying after the first few sentences. He did not reprimand me but, with a smile, encouraged me to get on with a difficult job.

"Having been at his elbow up to the publication of the 1948 *Pharmacopoeia* I can say without fear of contradiction that he undertook with cheerfulness and great zeal a more complex and laborious task than the preparation of any previous

Pharmacopœia, not excluding the original one of 1864. This was a task important not only to Great Britain but also to the Commonwealth countries and Colonies. For instance, special monographs were written on substances which had to withstand tropical heat. Gunn, and the equally devoted Hampshire, mastered the difficulties which incessant additions to knowledge impose on experts who are content with nothing less than perfection in their unsparing efforts to bring the *British Pharmacopœia* to the utmost possible level of completeness and accuracy."

Professor Gunn leaves a widow, two sons, and a daughter.

GEORGE SUTCLIFFE SEED

M.B. Leeds, F.R.C.S., D.L.O.

Mr. George Seed, whose death we announced earlier, was senior consulting aural surgeon to the General Infirmary and to St. James's Hospital, Leeds, and senior clinical lecturer in otology in the university.

He was born in Halifax on April 27, 1905, and received his early education there. He entered the Leeds Medical School in 1922, and qualified M.B. in 1927. His early resident appointments were at the Birmingham and Midland Ear and Throat Hospital. Later he returned to Leeds as resident aural officer to the General Infirmary, a post which he held for a record period of six years. He obtained the D.L.O. in 1930, and became an F.R.C.S. in 1936. He studied in Edinburgh and also in Vienna—and other European centres. This training equipped him admirably for his appointment in 1937 to the honorary staff of his own teaching hospital.

In 1938 he joined the Territorial Army as otologist to the 18th General Hospital which formed in Leeds. Soon after the outbreak of war he was with the British Expeditionary Force in France and he took part in the evacuation from Boulogne. Shortly afterwards he was posted to India; later he became consultant aural surgeon to the Army in India with the acting rank of brigadier.

While in India he conceived the idea, with Munro Black of Newcastle, of forming a North of England Otolaryngological Society, and in 1947 the inaugural meeting was held in Leeds. He was the first secretary and treasurer and arranged all the preliminary organisation. He became the president in 1952. Now fully established as one of the most active in the specialty, the society will always recall his foresight and his interest in his fellow surgeons, and the cooperation and good fellowship these evoked. Believing in seeing for himself and in personal contacts, he had been to all the leading ear, nose, and throat clinics in Europe, as well as some of those in the United States and Canada, and he was a frequent visitor to colleagues in this country. At the time of his death he had lately been elected vice-president of the otological section of the Royal Society of Medicine.

After the war Mr. Seed was the prime mover in increasing the number of consultants at the General Infirmary from two to three; and a colleague outside his specialty remarks that "throughout the history of the National Health Service it must surely be true that no three consultants worked more closely, and in greater harmony and friendship". He had instilled new vigour into the ear, nose, and throat department, and both in hospital and in private practice he showed "the gentleness and care that was the outstanding feature of his work, his surgical technique, and of his whole character". His operative technique was meticulous, delicate, and a delight to watch, and the new methods in otology, employing an operating microscope, suited his painstaking temperament.

His colleague, O. C. L., to whom we are indebted for much of the information in this memoir, writes:

"He enjoyed immensely attending clinical meetings, and, whilst he never said very much, when he spoke it was always to the point, full of wisdom, and, if the occasion demanded, witty; but his main delight on these occasions was to have little chats and discussions with a few of his many friends. As a lecturer he took great interest in student activities, and he was staff president of the Medical Society last year. Students loved him, and he was an immensely popular teacher. He made several important contributions to the specialist journals; he wrote a section on the œsophagus in *Diseases of the Ear, Nose and Throat*, edited by Scott Brown; and only recently he had completed a chapter on carcinoma of the larynx in a book which is to appear shortly. But his main interest was always the welfare and improvement of the ear, nose, and throat department of the Leeds General Infirmary.

"It is a great privilege to have worked with him, to have been inspired by his sincerity, integrity, and selflessness, and to have shared his friendship and trust. Success and fame did not change him. With his tremendous sense of humour, he was the most modest of men. He was ever and absolutely genuine, and this may have been the greatest of his many virtues."

Five years ago Mr. Seed became seriously ill; and his friends speak of the fortitude with which he bore a series of major operations, quickly returning to all his arduous duties. In recent years he had become a fisherman, and only a few days before his death he was on holiday in the North of Scotland where he caught his first salmon. His family life with his wife and three daughters was a great satisfaction to him.

ARTHUR THEODORE TODD

O.B.E., M.B. Edin., M.R.C.P.

MUCH of the work of Dr. A. T. Todd, physician to the Bristol Royal Infirmary, who died on Oct. 20, was concerned with the treatment of advanced malignant disease; and in the years between the wars he was a vigorous advocate of active forms of medical treatment for patients who had been pronounced incurable.

Born in 1888 in County Down, the son of a clergyman, he was educated at Latimer School, Queen's University, Belfast, and Edinburgh University, where he graduated with first-class honours in 1912. Later he served in the R.A.M.C. and acted as consulting physician to the Rhine Forces; and before his appointment to the Bristol Royal Infirmary he held a lectureship in pathology in the University of Bristol.

In the years following the 1914–18 war Todd became interested in the use of lead and selenium in the treatment of cancer. Blair Bell and his colleagues in Liverpool had been the first to give intravenous injections of colloidal lead to patients with malignant disease, but they were cautious in their statements about so toxic a substance. Todd used lead selenide and in the end he came to favour colloidal selenium alone. His work and that of others who studied this subject suggested that occasionally various compounds of lead in suitable doses could produce definite improvement, without the risk of the rapid deterioration in general physical condition that followed large doses of lead. Todd recommended that his regime of medical treatment, of which lead selenide was a part, be used in conjunction with irradiation and surgery. In 1936 an investigation of the colloidal selenium treatment of cancer by the medical committee of the Royal Cancer

Hospital produced discouraging results, but Todd maintained that the trial had not been conducted according to his methods.

His interests were by no means confined to malignant disease, and contributions from him on many different subjects appeared regularly in our correspondence columns. He wrote three books, *Treatment of Some Chronic and "Incurable" Diseases* (1937), *Medical Aspects of Growing Old* (1946), and *Good Living* (1954), in which his philosophical temperament was often manifest.

CHARLES MELTON OCKWELL

M.D. Lond., F.R.C.S., D.P.H.

Dr. C. M. Ockwell, who died in Guy's Hospital on Oct. 17, was widely respected for the many achievements of his varied career, and the readiness with which he shared his talents and wisdom.

Born in 1883, the son of Charles Ockwell, of Cricklade, Wiltshire, he entered Guy's Hospital in 1901 and qualified in 1906. While a student dresser to Mr. W. H. A. Jacobson, he contracted septicæmia at a postmortem and was operated on and personally attended by Mr. Jacobson day and night for many weeks. He intended taking up surgery, but this long illness made it impracticable and he entered general practice as a partner to Dr. M. W. Renton in Dartford. While in general practice he obtained three higher qualifications—F.R.C.S. in 1919, D.P.H. in 1920, and M.D. in 1933.

As he worked in an important munitions area, he was not accepted for service in 1914, but in 1915 he spent a year as surgeon at a base hospital at Fécamp. From 1916 until the end of the war he was ophthalmic surgeon at the Royal Herbert Hospital, Woolwich. He became medical officer of health for Crayford in 1921 and extended this work to include Swanscombe urban and Dartford rural district councils in 1926. Later he was appointed venereologist in the county of Kent, and with his other duties became a full-time public-health officer. Early in the 1920s he was instrumental in founding at Crayford one of the first maternity and antenatal centres; this work developed rapidly and soon an enlarged home was dealing with 700 maternity cases a year. He was one of the pioneers of diphtheria immunisation, and in 1929, within two years of the start of this project, over 70% of his child population had been immunised.

After Munich he trained the casualty services in North Kent, and this heavily bombed area benefited greatly by the very efficient service he constructed. During the late war he was exceptionally busy when a very large number of Service patients, as well as civilians, were referred to his clinics in several parts of Kent. Day after day he worked late into the night, returning to start a new day at another busy clinic. He still had time to develop an interest in dermatology, and he studied at Guy's and St. John's Hospital, Lisle Street, and undertook duties at Guy's and other hospitals. On the inception of the National Health Service in 1948 he became a consultant dermatologist and venereologist.

D. E. writes:

"When Dr. Ockwell officially retired seven years ago he married Kathleen Keirle, who, as his secretary and chauffeuse, had been his daily companion for over twenty years. They moved farther into the Kent countryside, building a house on the Pilgrims' Way, where they created a labour-saving garden of trees and shrubs which is only now maturing. In spite of his retirement and new interests, he maintained close contact with medicine and affairs and kept up to date by regularly attending medical meetings. Consequently his services as a locum were in great demand and he was fully occupied, particularly in the summer months (he worked at forty different hospitals in the past two years). If he had time to spare he could never refuse this help to a colleague.

"He was liked and respected wherever he went and his death has come as a great blow to his many friends and those who worked with him. His gracious manner and quiet dignity, his trust and integrity, endeared him to all who came in contact with him. He was a kindly man, an experienced and good doctor, and above all an English gentleman."

ALEXANDER MELLICK

B.Sc., M.D. Glasg., F.R.F.P.S., D.O.M.S.

Dr. Alexander Mellick, the Glasgow ophthalmic surgeon, died suddenly on Oct. 19 while still in his fifties.

He was educated at Allan Glens' School, Glasgow, and Glasgow University, where he graduated B.SC. in 1924 and M.B. in 1926. In 1931 he took the M.D., and he was elected F.R.F.P.S. in 1949. After graduation he was in general practice in London before returning to Glasgow, where he continued his practice in the East End. For a time he was a physician to the outpatient department of the Glasgow Royal Infirmary. About 1933, however, he became interested in ophthalmology and served on the staffs of both the Glasgow Eye Infirmary and the Ophthalmic Institution. He became full surgeon to the Infirmary in 1948.

During the late war he served in the R.A.M.C. with the rank of major, finally becoming command ophthalmologist, Scotland. His other appointments included ophthalmologist to the Southern General Hospital and to the Glasgow Fever Hospitals and Sanatoria. He was also surgeon-in-charge of the large orthoptic training school at the Glasgow Eye Infirmary.

A. McL. W. T. writes:

"Alec Mellick was a very lovable man whose quiet patience and courtesy made him a popular colleague. He loved the beautiful things: art, music, and literature all found a place in his life. He had a fine brain, and his knowledge of ophthalmic literature was extensive. Ophthalmology in Glasgow has lost a fine surgeon who will be greatly missed."

And a younger colleague, M. B. S., adds:

"It was an education, both medically and in a general sense, to work under Dr. Mellick. In his approach to patients he showed great sympathy, particularly for the shy, diffident person, and he rapidly gained their confidence. He was outstanding in his medical cases, where his vast knowledge and practical experience in general practice made him keenly aware of the patient's general health as well as his ocular condition. With ophthalmological problems, he had an uncanny ability for recollecting published articles (foreign as well as British) and he could often produce the apt reference from his private file of references.

"His appreciation of the arts was exceptional: he played the piano excellently and was a founder member of Glasgow's Chamber Music Society. He thus combined with unusual success a cultured outlook and a scientific approach to life."

Dr. Mellick leaves a widow.

HANS W. GRUHLE

M.D.

WITH the death of Professor Gruhle at the age of 78, the psychiatry of the German-speaking countries has lost one of the few survivors of its creative era, from which originated most of what is scientifically valid today in psychiatry.

Gruhle was a pupil of Kraepelin, and like his teacher was strongly interested in psychology as a scientific basis of psychiatry. As early as 1911 he pointed to the social implications of psychiatric illness and insisted on their importance in treatment of patients in hospital. He was a brilliant teacher and a prolific writer distinguished by critical clarity and precision of thought and style. A collection of selected writings (*Verstehen und Einfühlen*, 1953) demonstrates the breadth of his interests and knowledge, extending from the education of juvenile

offenders to the psychological æsthetics of the death mask. Gruhle wrote a textbook of psychiatry for the general practitioner during his Army service in the first world war. When banned from his academic position by Hitler, he concluded his chef-d'œuvre *Verstehende Psychologie* (1948), in which he welded psychological motivation and understanding between men with scientific evidence and method. This work will form the basis of debates of future generations on the philosophy of psychiatry. Its author will be sadly missed; for, in the words of a friend, he was the " living scientific conscience of German psychiatry ".

W. M.-G.

Diary of the Week

NOV. 2 TO 8

Monday, 3rd

UNIVERSITY OF LONDON
5.30 P.M. (London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.) Dr. Karl Evang (Norway): Main Types of Existing Health Services. (First of five Heath Clark lectures on Health Service, Society and Medicine.)

POSTGRADUATE MEDICAL SCHOOL, Ducane Road, W.12
4 P.M. Dr. Brian Ackner: Psychogenic Pain.

Tuesday, 4th

UNIVERSITY OF LONDON
5.30 P.M. (London School of Hygiene and Tropical Medicine.) Dr. Evang: Role of the Hospital. (Second Heath Clark lecture.)

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5.30 P.M. *Pathology.* Dr. R. H. Heptinstall: Renal Biopsies. Dr. Iain MacIntyre: Aspects of Magnesium Metabolism and Magnesium Deficiency. Dr. D. J. H. Payne: Epidemic Nephritis in North Yorkshire.
8.30 P.M. *Orthopædics.* Dr. Walter Blount (Milwaukee): Osteotomies of the Upper End of the Femur.

ST. MARY'S HOSPITAL MEDICAL SCHOOL, Paddington, W.2
5 P.M. Mr. Roger De Vere: Fibroids and Allied Tumours.

INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. P. F. Borrie: Cutaneous Vascular System.

INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
3 P.M. (Hammersmith Hospital, Ducane Road, W.12.) Dr. J. F. Goodwin: Heart-disease and Pregnancy.

Wednesday, 5th

UNIVERSITY OF LONDON
5.30 P.M. (London School of Hygiene and Tropical Medicine.) Dr. Evang: Role of the General Practitioner. (Third Heath Clark lecture.)

ROYAL SOCIETY OF MEDICINE
5.15 P.M. *History of Medicine.* Mr. Terence Cawthorne: The Last Illness of Oscar Wilde.

POSTGRADUATE MEDICAL SCHOOL
2 P.M. Dr. G. M. McGowan: Potassium Metabolism.

INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. R. W. Riddell: Subcutaneous Infections due to Fungi.

INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Dr. Paul Wood: Bedside Techniques in Cardiology.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, W.1
3.30 P.M. Dr. A. B. Stewart: London County Council Health Services.

ASSURANCE MEDICAL SOCIETY
5 P.M. (11, Chandos Street, W.1.) Dr. J. M. Campbell: Life Assurance for those Applicants with Heart-disease.

MIDLAND MEDICAL SOCIETY
8.15 P.M. (36, Harborne Road, Edgbaston, Birmingham, 15.) Dr. P. H. Davison: Management of Chronic Cardiac Failure.

MANCHESTER MEDICAL SOCIETY
5 P.M. (Medical School, University of Manchester.) *Medicine.* Dr. P. J. D. Snow: The Carcinoid Syndrome. Dr. Donald Longson: Adrenal Hyperfunction.

MEDICO-CHIRURGICAL SOCIETY OF EDINBURGH
8.30 P.M. (18, Nicolson Street, Edinburgh.) Sir Stanley Davidson: Travelogue, 1922–58.

Thursday, 6th

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S.W.1
5 P.M. Dr. K. W. Donald: Heart-disease and Exercise. (Bradshaw lecture.)

UNIVERSITY OF LONDON
5 P.M. (Royal Society of Medicine.) Prof. Luzius Rüedi (Zürich): Observations on the Histology and Functions of the Larynx. (Semon lecture.)
5.30 P.M. (London School of Hygiene and Tropical Medicine.) Dr. Evang: Role of Drugs. (Fourth Heath Clark lecture.)

ROYAL SOCIETY OF MEDICINE
8 P.M. *Neurology.* Dr. Alick Elithorn, Dr. Maurice Partridge, Mr. Wylie McKissock: Psychosurgery.

UNIVERSITY OF LIVERPOOL
5.15 P.M. (Old Medical School.) Dr. William Brockbank: The Ancient Art of Enema Administration.

ROYAL COLLEGE OF PHYSICIANS OF EDINBURGH, 9, Queen Street, Edinburgh, 2
5 P.M. Prof. W. Melville Arnott: Climate of Medical Education. (John Matheson Shaw lecture.)

Friday, 7th

ROYAL COLLEGE OF OBSTETRICIANS AND GYNÆCOLOGISTS, 58, Queen Anne Street, W.1
4 P.M. Dr. J. M. Crawford: Study of Placental Growth in Normal Pregnancy and in Erythroblastosis Fœtalis. (William Blair-Bell lecture.)

UNIVERSITY OF LONDON
5.30 P.M. (London School of Hygiene and Tropical Medicine.) Dr. Evang: Public Health Service. (Fifth Heath Clark lecture.)

ROYAL SOCIETY OF MEDICINE
10.30 A.M. *Otology.* Mr. Terence Cawthorne: Vertigo. (Presidential address.)
2.30 P.M. *Laryngology.* Mr. R. L. Flett: Pharyngitis. (Presidential address.)
5.30 P.M. *Anæsthetics.* Prof. J. H. Burn: Pharmacological Investigation of Anæsthetic Drugs for Clinical Trial.

POSTGRADUATE MEDICAL SCHOOL
10 A.M. Mr. A. S. Kerr: Relief of Pain.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
3.30 P.M. Mr. G. H. Howells: Sinusitis.

MANCHESTER MEDICAL SOCIETY
4.30 P.M. (Clinical Sciences Building, York Place, Manchester.) Sir Roy Cameron: The Principle of Reversibility in Liver Pathology.

ROYAL MEDICO-CHIRURGICAL SOCIETY OF GLASGOW
8.30 P.M. (242, St. Vincent Street, Glasgow, C.2.) Mr. Thomas Gibson: Domestic Burns—Their Prevention and Treatment. Mr. Ian MacGregor: The Changing Pattern of Treatment in Hand Infections.

Saturday, 8th

INSTITUTE OF LARYNGOLOGY AND OTOLOGY
11.30 A.M. Professor Rüedi (Zürich): New Developments in the Surgery of Otosclerotic Diseases.

Appointments

ARON, K. W., M.B. Brist., D.P.M.: consultant child psychiatrist to develop child-guidance services, Glamorgan.
CLARK, D. W., M.B. Lond., F.F.A.R.C.S.: consultant anæsthetist, Leeds General Infirmary and Regional Board hospitals.
FRIZELLE, G. M., M.D. Belf., D.P.H.: M.O.H., East Hertfordshire.
TYSER, P. A., M.D. Lond.: county M.O. and principal school M.O., Cambridgeshire.
WELCH, G. E., M.B. Durh., D.P.H.: M.O.H. and deputy principal school M.O., Leeds.

Birmingham Regional Hospital Board:

JENKINS, A. V., M.B. Lond., F.F.A.R.C.S.: consultant anæsthetist, Birmingham (Selly Oak) group of hospitals.
SEWELL, WILLIAM, M.B., F.R.C.S.: part-time consultant surgeon, Stoke-on-Trent group of hospitals.
TRAFFORD, H. S., M.B. Manc., F.R.C.S.E., D.OBST.: consultant surgeon, Stoke-on-Trent group of hospitals.

School Health Service, Birmingham:

BOISEN, DOROTHY M., M.B. Brist.: M.O.
O'CONNELL, SUSAN, M.B. N.U.I., D.P.H.: M.O.
WALKER, AUDREY M., M.B.: M.O.

Colonial Appointments:

ASREGADOO, E. R., M.D., B.SC., D.O.: junior ophthalmologist, British Guiana.
CHANDY, G., L.M.S.S.A., D.T.M. & H.: M.O., British Guiana.
CHENG, G. K.-K., M.D. Shanghai, T.D.D.: tuberculosis specialist, Hong Kong.
CLARKE, VINCENT, M.B. Sheff.: M.O., Kenya.
COX, D. A., L.M.S.S.A.: M.O., Jamaica.
DE COUTERE, I. A. A., M.B. Lond., M.O., Northern Region, Nigeria.
HEINE, B. E., M.B. N.Z., D.C.H.: travelling M.O., Sarawak.
HELBERT, DAVID, M.D. Lpool: M.O., Hong Kong.
HILLS, M. M., M.B. Birm.: M.O. Jamaica.
HUNTER, F. G., M.B. Lond.: M.O., Northern Region, Nigeria.
KREDEL, E. W. K., M.D., M.P.H.: M.O.H., British Honduras.
LU, MOXGAN, K. C., M.D., B.SC.: thoracic surgery specialist, Hong Kong.
MASSIAH, L. R., M.B. Glasg.: M.O. (Grade C), Trinidad.
ONG GUAN BEE, M.B. Hong Kong, F.R.C.S., surgeon specialist, Hong Kong.
PEARCE, J. A., M.B. Dubl.: medical superintendent, Nigeria.
PHILLIPS, B. L. C., M.B. Lond., M.R.C.P.: medical specialist, Hong Kong.
POON, YEE KIT, L.R.C.P.E., F.F.A. R.C.S., D.A.: specialist in anæsthetics, Hong Kong.
ROBERTS, A. L. K., M.B.: M.O., Kenya.
STEWART, J. P., L.R.C.P.I.: M.O., Uganda.
TUCKETT, R. F., M.B. Cantab.: M.O., Tanganyika.
WEN, HSIANG LAI, M.D., M.C.P.S. Manitoba: specialist in neurosurgery, Hong Kong.
WHITLAM, J. C., M.B. Aberd.: M.O., Sarawak.
WONG, W. L., M.D. Shanghai, D.M.R.D.: specialist in diagnostic radiology, Hong Kong.
WYLIE, G. B., M.B. Glasg., F.R.C.S.E.: medical superintendent, Cunningham Hospital, St. Kitts, Leeward Islands.

Births, Marriages, and Deaths

BIRTHS

PERRY.—On Oct. 19, at the County Hospital, Haverfordwest, to Dr. Elizabeth Perry (née Thomas), wife of Dr. Lynn Perry—a daughter, sister for William and David.

DEATHS

OCKWELL.—On Oct. 17, at Guy's Hospital, Charles Melton Ockwell, M.D., F.R.C.S., aged 74, of The Coppice, Pilgrims' Way, Kemsing, Kent.

Notes and News

A NEGLECTED ARMY

OF the lingering relics of modern war, perhaps none is more tragic than the ragged army of displaced persons. Of the million or so of these people in Europe at the end of the 1939–45 war, most have been absorbed into one or another of the Western nations. But there remain some ninety thousand who have not been accepted, owing to old age or to illness—sometimes affecting only one member of a whole family. These people, cut off from their past and promised no future, eke out their days in a permanent transit camp; and if they are not yet gripped by despair it is largely because of the efforts of voluntary agencies. One such agency in this country is the Adoption Committee for Aid to Displaced Persons.

Founded in 1953, this body set about its task in workmanlike fashion. Perceiving that the two most immediate needs of these refugees were human contacts and elementary physical comforts, it sought to secure both these by fostering a scheme under which families in Britain "adopt" persons or families in German camps. With this scheme well launched, the committee has turned its attention to restoring individuals and groups to the outside world by, for example, the offer of vocational training. Finally the committee, with the authority of its extensive experience, is adding its voice to those who are seeking to muster national and international opinion in favour of the only satisfactory permanent solution—namely, the full incorporation of these people into national life.

The committee carries on these activities with resources that do not suffice for even the most pressing claims. Those sympathising with its objectives can help by buying Christmas cards, obtainable at 6*s.* 6*d.* a dozen post free from the Adoption Committee for Aid to Displaced Persons, 227, Edgware Road, London, W.2.

GULBENKIAN GRANTS

GRANTS decided this year by the Calouste Gulbenkian Foundation amount to nearly £1 million, of which over £200,000 goes to the British Commonwealth. Some of them are quite small; but they are refreshingly diverse, giving encouragement to many unconventional but promising projects.

The Foundation is specially concerned with Portugal, where it has its headquarters, and several substantial grants are made to Portuguese medical institutions. The Lisbon civic hospitals receive £21,775, the Centre for Research in Infectious Diseases £12,850, the Egaz Moniz Research Centre £3750 for fellowships, and the Institute of Social Cardiology £12,500. The anti-tuberculosis service in Mozambique gets £26,250 for three mobile mass-radiography units.

Educational grants in Britain include £50,000 to the prospective Churchill College, Cambridge, to endow three Gulbenkian studentships for graduates from overseas, £12,000 for an additional centre for the Outward Bound Trust, and £3000 to the Oxford University department of education for a study of specialisation in schools and its relevance to university requirements. (Mr. Alec Peterson, a former headmaster, is invited to draft an ideal syllabus and time-table for a combined arts and science VIth form.)

The National Old People's Welfare Council, in London, is given up to £500 for an experimental course for middle-aged people on adjustment to ageing and sensible planning for retirement; the Family Welfare Association (formerly the Charity Organisation Society) £5000 for an independent re-examination of family case-work in the Welfare State; the Ockendon Venture (Woking) £4500 for the education in England of six children born to the "hard core" of displaced persons on the Continent; Ambridge House Trust (London) a loan of £2000 to buy a house for continuing and expanding the work (begun by Mrs. Jack Ambridge singlehanded) of taking in unmarried or deserted mothers and their babies after they leave hospital; Stevenage New Town up to £1000 for an inquiry into the needs of the town's adolescents, whose number will rise from 1600 to about 9000 in fourteen years' time; the Elfrida Rathbone Committee £300 a year for three years to start a club for educationally subnormal girls leaving a special school; and the Prison Commission £150 a year for three years for resettling youths discharged from detention centres.

The United Kingdom and British Commonwealth branch of the Foundation has its office at 3, Prince Albert Road, London, N.W.1. Its secretary is Mr. Allen Sanderson.

DISABLEMENT PENSIONERS AND UNEMPLOYABILITY SUPPLEMENTS

MEDICAL certificates of incapacity for work will no longer be needed by the small number of the severely disabled war and industrial-disablement pensioners who are getting an unemployability supplement in addition to their basic pensions.

A pensioner being paid the unemployability supplement cannot at the same time draw national insurance sickness benefit. Nevertheless in the past he has had to obtain periodic medical certificates from his doctor and to send them to the local Pensions and National Insurance office to qualify for national insurance contribution credits to keep his insurance record fully in credit. The Ministry of Pensions and National Insurance has now arranged in these cases for a review of the medical evidence already obtained in connection with the award of the disablement pension. When it appears that further certificates are unnecessary, the pensioner will be sent a letter telling him this and advising him to show the letter to the doctor who has been issuing his certificates.

University of Oxford

On Oct. 16 the degree of B.M. was conferred on the following: G. O. M. Jones, F. S. Plumpton, Gillian M. Shaw (in absentia).

University of Leeds

Dr. D. B. Bradshaw has been appointed to the chair of public health from Oct. 1 this year in succession to Prof. I. G. Davies, who has resigned.

Dr. Bradshaw qualified M.B. in the University of Dublin in 1932, when he gained the Mercer's Hospital gold medal. He took the D.P.H. at Dublin in 1935, gaining the De Renzy prize in public health. In the 1939-45 war he served in the R.A.M.C., reaching the rank of lieut.-colonel. In 1946 he was awarded the Swedish Red Cross medal for public-health work in Germany; and, before returning to this country, he was principal control officer of the public-health section at the headquarters of the Military Government in Hamburg. After serving as deputy medical officer of health for South Shields he came to Leeds in 1948 as deputy medical officer of health and deputy school medical officer, and lecturer in public health in the university. His appointment as medical officer of health was announced earlier this year. He has published articles on serological aspects of various infectious diseases.

Dr. M. W. Atkinson has been appointed senior registrar and tutor in psychiatry, Mr. R. G. Burwell lecturer in anatomy, Dr. A. J. Kenny lecturer in biochemistry, Dr. N. R. Rowell senior registrar and tutor in dermatology, and Mr. F. G. Smiddy lecturer in surgery.

University of Edinburgh

Dr. Katherine M. Levy has been appointed assistant in the department of public health and social medicine.

Royal College of Physicians of London

On Tuesday, Nov. 18, at 5 P.M., at the college, Pall Mall East, S.W.1, Dr. Mildred Creak will give the Charles West lecture. She will speak on Child Health and Child Psychiatry—Neighbours or Colleagues?

Royal College of Surgeons of Edinburgh

At the annual meeting of the college, held on Oct. 15 the following office-bearers were elected for the coming year:

President, Prof. John Bruce; vice-presidents, Prof. Norman Dott and Mr. W. W. Galbraith; secretary, Mr. C. W. A. Falconer; treasurer, Mr. J. J. Mason Brown; president's council, Mr. David Band, Mr. R. S. Barclay, Mr. J. R. Cameron, Mr. I. L. Dick, Prof. D. M. Douglas, Mr. E. L. Farquharson, Mr. A. J. C. Hamilton, Mr. J. N. J. Hartley, Prof. R. J. Kellar, Mr. J. A. Ross, Prof. G. I. Scott, Mr. J. A. Shepherd, Mr. R. L. Stewart; representative on the General Medical Council, Mr. K. Paterson Brown; conservator of museum, Prof. D. E. C. Mekie; convener of museum committee, Prof. R. J. Kellar; hon. librarian, Dr. Douglas Guthrie.

The honorary fellowship was conferred on Prof. Charles B. Huggins (Chicago).

The following were admitted to the fellowship:

Jack Abrahamson, W. R. Allan, Lynne W. Baker, D. B. Berryman, Kamta Shanker Bhargave, Nirmalendu Bhattacharyya, Rowland Cowley, S. J. Crews, P. J. E. Cruse, Barin Kumar Datta, Bhabit Dawka, Navin Chandra Desai, Hugh Dovey, G. H. Dunstone, H. M. El-Sayed, K. D. Glass, Ghanshyam Das Goel, A. J. Grant, Pushpa Gupta, Mohsmed Habibulla, Percival Harnarayan, F. W. Harrison, E. T. Heath, A. W. B. Heywood, H. K. Ismail, N. D. Jeyasekharan, M. J. Killingback, H. M. Learoyd, J. E. Lorang, M. H. Luntz, M. J. Lyons, Maher Mahran Ahmed Mahran, F. P. S. Marriott, Pravinchandra Ratilal Mehta, D. N. Menzies, R. E. Mickel, D. M. Millar, Makesh Chandra Misra, Sudhansu Ranjan Mitra, Bijay Chandra Mukerjee, Vinayak Ganpat Muzumdar, D. W. Pfanner, Robert Pringle, D. C. Provan, P. A. Rachow, J. A. Ryan, Manoutchre Sabetian, Chandramma Dayananda Sagar, Krishnalal Mansukhlal Shah, Rameshwar Prasad Singh, J. G. Smith, J. H. Tait, Cheok Fai Tham, T. T. Thomas, Mokkilmaruthur Vasudevan, N. H. Welsh, Thomas Wilson.

Royal College of Physicians of Ireland

The following officers have been appointed for 1958–59:

President, Dr. P. T. O'Farrell; vice-president, Dr. M. Crowe; censors and examiners, Dr. E. B. McEntee, Dr. M. I. Drury, Dr. E. W. L. Thompson, Dr. M. Crowe; representative on the General Medical Council, Dr. Edward T. Freeman; registrar, Dr. Charles Dickson; treasurer, Dr. Geoffrey Bewley.

University of Otago

Dr. C. W. Dixon, reader in epidemiology in the University of Leeds, has been appointed to the chair of social and preventive medicine in the university.

Royal Australasian College of Physicians

At a meeting of the council in Melbourne on Oct. 9 the following were admitted to membership:

W. Berns, J. F. T. Croll, J. C. Farrell, H. G. Gallagher, B. R. Huxtable, K. P. W. Moore, T. Selby (New South Wales); N. McK. Bennett, R. A. Chenoweth, A. E. Doyle, A. D. Grounds, F. L. Johnson, D. S. Nurse, R. G. Shaw, L. E. G. Sloan, B. M. Spence, J. B. Webb, C. W. E. Wilson (Victoria); B. J. Knapp, J. P. Masel (Queensland); I. J. Forbes, J. G. Wilson (South Australia). J. A. Bonnin (South Australia) and K. V. Smith (New South Wales) were admitted under the special provisions of article 37.

National Association for Maternal and Child Welfare

The annual conference of this association will be held at Church House, Westminster, London, from July 21 to 23, 1959. Further particulars may be had from the secretary of the association, Tavistock House North, Tavistock Square, W.C.1.

Royal Commission on Doctors' and Dentists' Remuneration

The Royal Commission will hold a public hearing on Tuesday, Nov. 4, at 10, Carlton House Terrace, London, S.W.1. Representatives of the Executive Councils' Association (England) have been invited to attend. The hearing will begin at 11 A.M.

National Council for the Unmarried Mother and Her Child

At a meeting to be held on Thursday, Nov. 20, at 2.30 P.M. at County Hall, Westminster Bridge Road, London, S.E.1, the subject will be Who Are We Helping? Lord Gorell, the president, will take the chair, and the speakers will be Dr. James Hemming, Dr. Catherine Morris Jones, and Miss E. M. Steel. The council's address is 21, Coram Street, W.C.1.

Society of Medical Officers of Health

At the annual dinner of the society in London on Oct. 23, Mr. Derek Walker-Smith, Minister of Health, thanked medical officers of health throughout the country for their help in promoting the success of the poliomyelitis vaccination programme. But a greater response from parents was still needed, he added, for nearly half of them had not yet registered their children for vaccination; and medical officers of health could do much to persuade both parents and the young people to whom the scheme was now extended of the importance of vaccination. The Minister also spoke of "another great contemporary problem", mental health. Legislation would soon be introduced to implement some of the recommendations of the Royal Commission on Mental Illness and Mental Deficiency, and local authorities would be further expanding their mental health services. The emphasis would shift to community care, which could ease the burden on hospitals. The Minister was proposing The Society, for whom the president, Dr. J. A. Stirling, replied. He urged the Minister to make known more widely the safety of the Salk vaccine, which was "doing the job very well". Indeed publicity measures might be fortified all round if an experience of Dr. Stirling's was anything to go by. A medical officer told him of the mother who said she did not believe in vaccination because "both her children had been immunised and neither of them took it". Dr. George Gibson proposed The Guests, and in his reply Sir Kenneth Cowan, chief medical officer of the Department of Health for Scotland, spoke enthusiastically of the work Dr. Stirling had done for the society and medical officers of health in general. Sir Kenneth deplored the title Cinderella of the Profession so often applied to the M.O.H. and sought to change it to Prince Charming.

King's College Hospital Medical School

Queen Elizabeth the Queen Mother, chancellor of the University of London, will open the new extension to the medical school at 3 P.M. on Tuesday, Nov. 4.

Royal Society of Medicine

The Rockefeller Foundation has made a grant of £24,000 to the Royal Society of Medicine for the support of the society's library over a period of five years or more, while endowment is being sought to ensure the library's continuing service and proper maintenance.

Richard Bright Centenary

The centenary of the death of Richard Bright will be commemorated at Guy's Hospital, London, S.E.1, on Monday, Dec. 1. At 2.15 P.M. there will be a combined round on Bright's disease and at 5 P.M. Prof. M. L. Rosenheim will give the Bright lecture on the Syndromes of Bright's Disease. Tickets may be had from the dean of the medical school.

On Tuesday, Dec. 2, at 2.30 P.M., at the Institute of Diseases of the Chest, Brompton Hospital, London, S.W.3, a discussion for general practitioners will be held on Virus Infections of the Respiratory Tract. The speakers will be Dr. F. O. MacCallum, Dr. J. C. McDonald, Dr. N. C. Oswald, and Dr. J. G. Scadding. Practitioners wishing to attend should notify the dean at the Institute.

On Wednesday, Nov. 19, at 6.30 P.M., a discussion on Presenting Medicine to the Public on Television will be held at the Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2. This discussion has been arranged by the medical section of the Scientific Film Association.

On Friday, Nov. 14, at 4.30 P.M., at the Institute of Laryngology and Otology, 330, Gray's Inn Road, London, W.C.1, Mr. T. G. Wilson will give the annual address on the Modern Treatment of Deafness in Historical Perspective. The annual dinner will be held in the evening at University College, Gower Street, W.C.1.

A meeting for general practitioners will be held on Sunday, Nov. 2, at 10.15 A.M., at University College Hospital, London, W.C.1. Dr. K. E. Harris will speak on cardiac irregularities, their significance and treatment.

The Family Planning Association has arranged with a number of medical schools for lectures to be given to students on sex in marriage. The first of these was given by Dr. Eleanor Mears in Leeds last week.

Prof. Ian Aird has been elected an honorary fellow of the Swedish Surgical Society and has been awarded the Olof Af Acrel medal of the society.

Prof. W. A. Bain is to resign the chair of pharmacology at the University of Leeds and is to take up the appointment of director of the Smith Kline & French Research Institute.

Sir Harry Platt left for India and Ceylon on Oct. 30, on a lecture-tour arranged by the British Council. He will visit centres in India, Pakistan, and Ceylon, and will return to the United Kingdom early in January.

A semi-permanent exhibition will be held from Nov. 5 to 26, at the Institute of Dermatology, Lisle Street, W.C.2, on the skin and friction.

CORRIGENDA: *Blankets and Infection.*—In the letter by Mr. A. W. Bayes (Oct. 25, p. 907) we unfortunately introduced errors into the third paragraph. This should begin: "Secondly, towelling, whether called tufted, turkish, or terry, is all basically the same weave. The adjectives turkish and terry are synonymous, but tufted is technically incorrect."

Hookworm and Anæmia.—At the foot of the letter by Dr. Holmes and Dr. Darke (Sept. 6, p. 529) we gave an outdated title for the institute which is now known as the East African Institute for Medical Research.

QUICKLY READY TO HAND

London Hospital Catgut in non-splintering 'spot' tubes

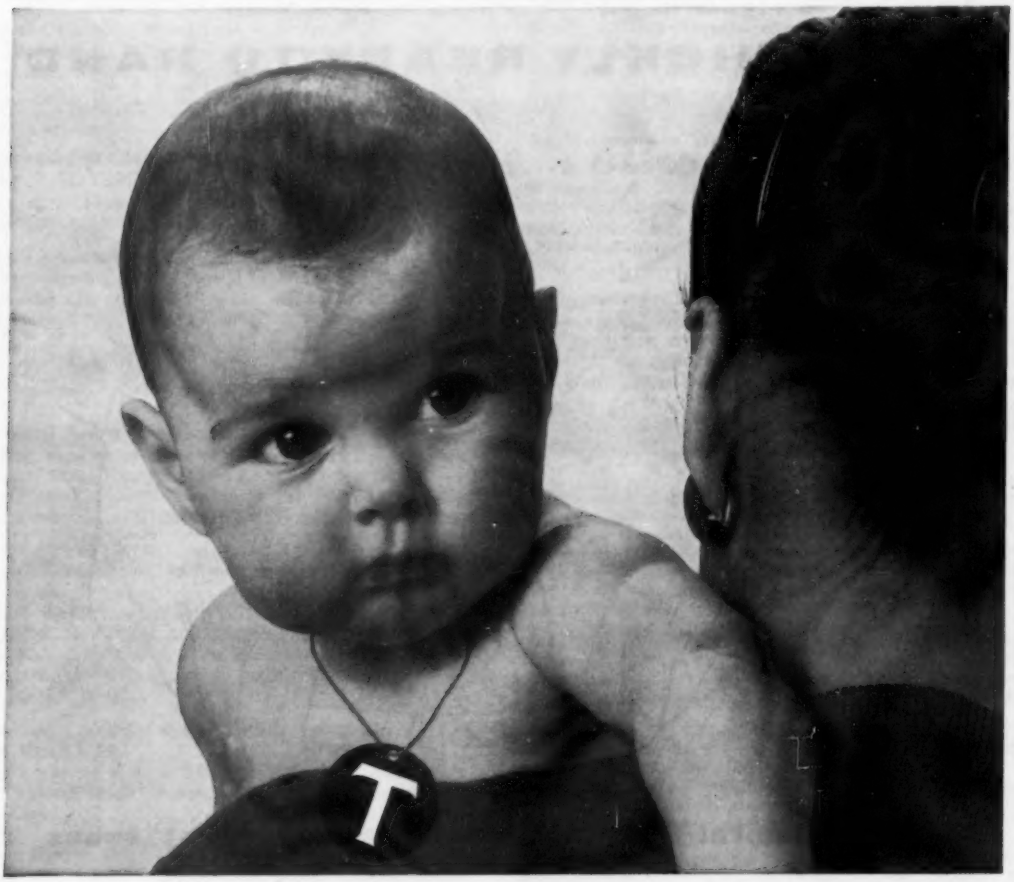
Speed is a matter of urgency in the Operating Theatre—which is why the London Hospital 'spot' tubes are so popular. Just a slight pressure, and instantly the tube breaks cleanly at the 'spot' position, and the sterilised suture is ready for use.

These are the advantages :

- The spot indicates the exact breaking point of the tube.
- If the thumbs are placed about ¾" apart, exactly opposite the spot, the tube breaks cleanly and easily under slight pressure.
- No filing is needed, no instruments required, no need to hold the tube in a swab.
- There are no dangerous glass splinters.

Always use **London Hospital Catgut**

the more F·L·E·X·I·B·L·E Suture



The problem of a substitute for breast milk, where a mother is unable to feed her baby herself, is most satisfactorily solved by giving Humanised Trufood. This is not an ordinary dried milk; it is cows' milk so modified that it closely resembles the natural food that a normal infant should have from birth. As in human milk, lactose is the only carbohydrate present. The ratio of casein to soluble protein, as well as the total protein content, is remarkably close to that in human milk; and the high emulsification of the full fat content ensures perfect reconstitution. Further information can be obtained from Trufood Limited, 113 Newington Causeway, London, S.E.1.

TRUFOOD *Formulated Baby Foods*

HUMANISED TRUFOOD · SPOONFOODS · TRUFOOD CEREAL FOOD

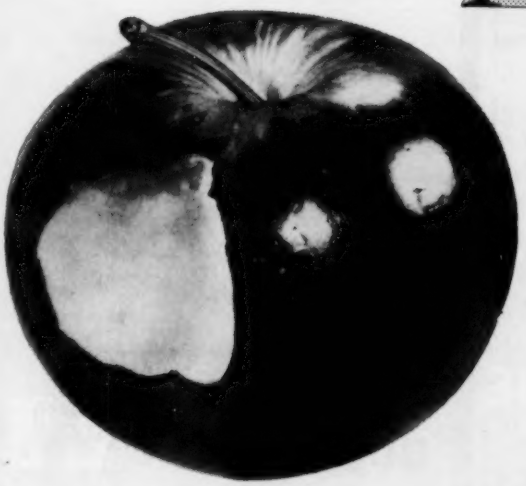
TFD 100-7249 100

In hepatic conditions . . .

In hepatic conditions, when a reserve of liver glycogen and the speedy ingestion of nourishment are of supreme importance, Lucozade is strongly indicated. Its many-sided appeal ensures immediate acceptance; and the fact that the patient will easily take as much as is necessary ensures an adequate blood sugar level in the shortest possible time.

Lucozade is lightly carbonated with an attractive golden colour and a pleasant citrus flavour. It contains 23.5% w/v Liquid Glucose B.P., and its energy value is 21 calories per fluid ounce. It is supplied in 6 oz. and 26 oz. bottles.

LUCOZADE



AN APPLE A DAY may keep the doctor away. But when his attention *is* required a special diet can shorten illness, save visits and allay the perplexities about food which often disturb those responsible for the patient's management.

Comprehensive services in dietary problems are available free of charge to the medical profession and include: a desk filing box containing an indexed supply of standard diets; preparation of special diets to suit individual needs; personal consultations with a dietitian. Please write for full details to:
The Secretary.

THE ENERGEN DIETARY SERVICE

25a BRYANSTON SQUARE · LONDON W1 · TELEPHONE AMBASSADOR 9332

35

An ultraviolet microscope used in Cancer Research.

An Appeal for Cancer Research

The Imperial Cancer Research Fund is the pioneer cancer research organisation and was brought into being in 1902 by the Royal College of Physicians and Surgeons to undertake systematic investigations into the causes, prevention and cure of cancer.

At present, in laboratories at Mill Hill, and at Lincoln's Inn Fields, the Fund employs twenty qualified experts in scientific research and fifty expert technicians and assistants. Visiting research workers from all over the world visit the Fund's laboratories.

Present-day cancer research calls for a very considerable expansion of the Fund's activities. New laboratories, adjoining the Royal College of Surgeons, are shortly to be built. In this undertaking, the Fund, which receives no official help and relies upon the public for support, is facing an immense task. A sum of £1,000,000 is needed to build and equip the laboratories which will be the most advanced cancer research centre in Europe.

IMPERIAL CANCER RESEARCH FUND

PATRON: HER MAJESTY THE QUEEN

Please help us generously
and send your gift to the Hon. Treasurer,
A. Dickson Wright, Esq., M.S., F.R.C.S.,
at Royal College of Surgeons,
Lincoln's Inn Fields, London, W.C.2.

'A splendid nightcap
and it's nourishing too!'

Bourn-vita is made from malt, milk, sugar, cocoa and eggs

sleep sweeter
BOURN-VITA
made by CADBURYS

Rough throats sorely need...

Rapidly active, safe and convenient for adults and children alike, Formacaine swiftly allays the discomfort associated with infections of the throat. Its two local anaesthetics—benzocaine and orthocaine—relieve the irritation of sensory nerve endings; its systemic sedative, codeine, helps to control cough and to relieve the general malaise that so often attends throat infections; its well recognised antiseptics—paraformaldehyde and menthol—counter the infection and cool inflamed tissues. Relief is prompt and prolonged . . . the tablets are easy and pleasant to take.

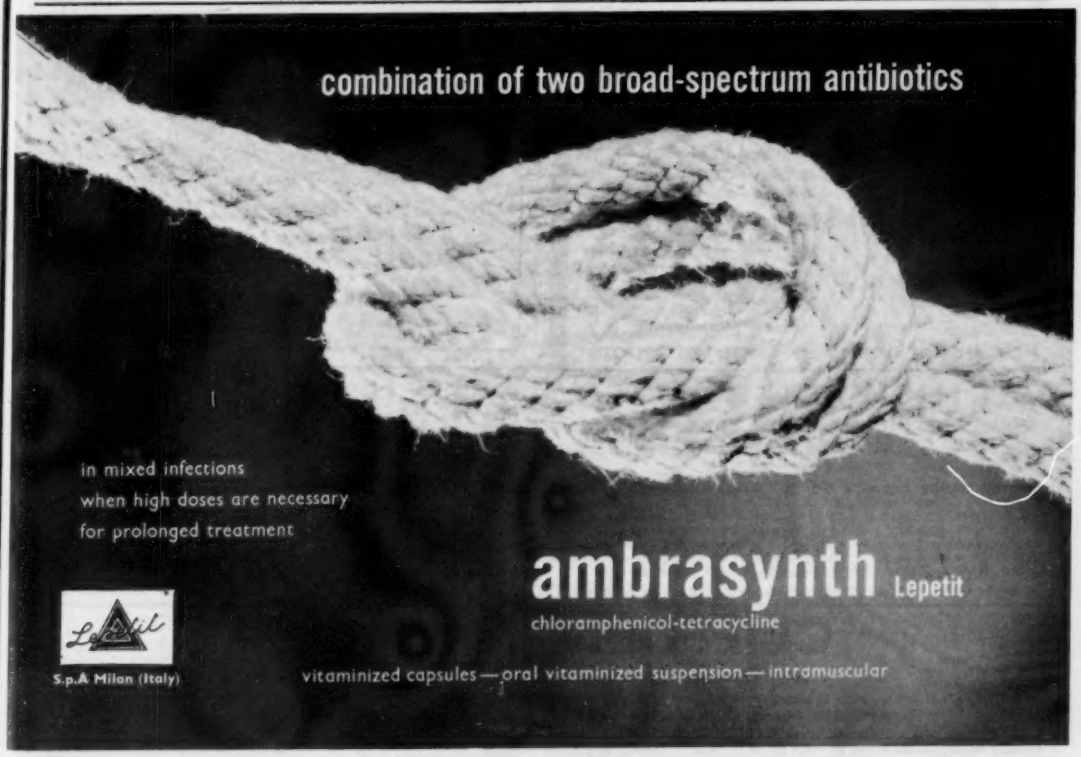
FORMACAINE

Surface—Anaesthetic Throat Tablets

Formula: Benzocaine ¼ grain, Orthocaine ¼ grain, Codeine Phosphate 1/24 grain, Paraformaldehyde 3/20 grain, Menthol 1/24 grain, Flavouring and Sugar base to 15½ grains.

In tubes of 20 tablets; also dispensing packs. Price 2/8½d. per tube. Basic cost to N.H.S. 1/6d. per tube.

THERAPEUTIC PRODUCTS LTD
67 Wigmore Street, London, W.1



H. K. LEWIS & Co. Ltd.

MEDICAL PUBLISHERS AND BOOKSELLERS

TEXTBOOKS AND WORKS IN MEDICINE, SURGERY AND ALLIED SCIENCES OF ALL PUBLISHERS
Catalogues sent on request. Please state interests.

FOREIGN BOOKS: Continental and American books obtained to order.
SECOND-HAND BOOKS: A constantly changing large stock of Medical and Scientific Literature available.

MEDICAL AND SCIENTIFIC LENDING LIBRARY
Annual Subscription from £1 17s. 6d. Prospectus on application

THE LIBRARY CATALOGUE revised to December, 1956, containing Classified Index of Authors and Subjects. Pp. xii + 1178. To Subscribers, £1 5s. net; to non-subscribers, £2 2s. net, postage 2s.

H. K. LEWIS & Co. Ltd., 136 GOWER STREET, LONDON, W.C.1. Phone: EUSton 4282

MOTORISTS

Perfect protection costs less with Boots Antifreeze

Be prepared for the sudden, sharp frosts of winter—put Boots Radiator Antifreeze in your car now.
Boots Antifreeze gives your car *complete* protection against both frost and corrosion. Get yours now*.

See how much less Boots Antifreeze costs:

1 QUART (enough for most small cars) **10/-**
3 PINTS (the new medium-car size) **15/-**
½ GAL. (protection at 4/9 a pint) **19/-**
OR 1 PINT 6/3 AND 1 GALLON 37/-
Containers free and non-returnable

* *Remember there is a special discount for doctors at* Boots THE CHEMISTS

For better value — shop at Boots

Photocopying

equipment ideally suited for use in
• TEACHING & RESEARCH
• LIBRARIES • COPYING
ANYTHING ANYWHERE

The Contoura Photocopier was designed for efficiency at copying pages in books and periodicals, without loss of effectiveness with single sheets. The Contoura translucent air-cushion gives perfect contact on curved pages, simply and easily; and limitations of size and bulk are eliminated by placing the Contoura on top. Prices are right, too.

CONTOURA Photocopiers Quarto £12/19, Foolscap £18/30, Double-Foolscap £29/42.
CONSTAT Processors (copies in 40 secs. by the "transfer" method) 9" £20, 14" £27.
Write or telephone to
CONTOURA PHOTOCOPYING LTD.,
56 Islington Park Street, London, N.1. (CAN 7900.)

DISABILITIES
AND HOW TO LIVE WITH THEM

By 55 Patients

"This is a new sort of textbook; unlike most other textbooks it is subjective, warm and human."—Review in *Nursing Times*

Demy 8vo. 252 pages. Price **10s. 6d.** *net (plus 10d. postage)*

THE LANCET LIMITED
7, Adam-street, Adelphi, London, W.C.2

CHISWICK HOUSE
PINNER, MIDDLESEX
Telephone: PINNER 234

Private Nursing Home for Nervous and Mild Mental Disorders and Alcoholism. Psychotherapy, E.C.T., modified insulin, etc. Fees from 18 guineas a week inclusive of nursing and medical attention. Forty patients of both sexes including a small number of long-term elderly cases. Two country houses in 5 and 6 acres respectively in adjoining grounds. Twelve miles north-west of London. Easily accessible by Metropolitan train from Baker Street to Pinner. Ten minutes' walk from Pinner station.

Apply to the Medical Director, DOUGLAS MACAULAY, M.D., D.P.M.

SPRINGFIELD HOUSE
Phone: BEDFORD 3417 **Near BEDFORD**
for MENTAL CASES (including the aged)
Fees from Ten Guineas per week.
For forms of admission, &c., apply to the Resident Physician CEDRIC W. BOWER.
INTERVIEWS IN LONDON BY APPOINTMENT.

CLIFFDEN, TEIGNMOUTH

For the early treatment of nervous disorders and patients needing rest and care

A well-appointed House with spacious balconies and extensive views of the South Devon Coast. Beautiful garden and own dairy in 35 acres In the same grounds, **ROWDENS**, a comfortable house with lovely views. Private road to the beach
There is also a charming house, **EBWORTHY, MANATON, DARTMOOR**, situated in 25 acres, 1100 ft. up for bracing moorland air
Resident Physicians—BERTHA M. MULES, M.D., B.S. ANNE S. MULES, M.R.C.S., L.R.C.P. *Telephones*—TEIGNMOUTH 289 and 537

ST. ANDREW'S HOSPITAL

FOR NERVOUS AND MENTAL DISORDERS

NORTHAMPTON

PRESIDENT : THE EARL SPENCER

MEDICAL SUPERINTENDENT : THOMAS TENNENT, M.D., F.R.C.P., D.P.H., D.P.M.

This Registered Hospital is situated in 130 acres of park and pleasure grounds. Voluntary patients, who are suffering from incipient mental disorders or who wish to prevent recurrent attacks of mental trouble ; temporary patients, and certified patients of both sexes are received for treatment. Careful clinical, biochemical, bacteriological, and pathological examinations. Private rooms with special nurses, male or female, in the Hospital or in one of the numerous villas in the grounds of the various branches can be provided.

WANTAGE HOUSE. This is a Reception Hospital in detached grounds with a separate entrance, to which patients can be admitted. It is equipped with all the apparatus for the complete investigation and treatment of Mental and Nervous Disorders by the most modern methods : insulin treatment is available for suitable cases. It also contains Laboratories for biochemical, bacteriological and pathological research. Psychotherapeutic treatment is employed when indicated.

MOULTON PARK. Two miles from the Main Hospital there are several branch establishments and villas situated in a park and farm of 650 acres. Milk, meat, fruit, and vegetables are supplied to the Hospital from the farm, gardens, and orchards of Moulton Park. Occupational therapy is a feature of this branch, and patients are given every facility for occupying themselves in farming, gardening, and fruit growing.

BRYN-Y-NEUADD HALL. The seaside home of St. Andrew's Hospital is beautifully situated in a park of 330 acres, at Llanfairfechan, amidst the finest scenery in North Wales. On the North-West side of the Estate a mile of sea coast forms the boundary. Patients may visit this branch for a short seaside change or for longer periods. The Hospital has its own private bathing house on the seashore. There is trout-fishing in the park.

For terms and further particulars apply to the Medical Superintendent (TELEPHONE : Northampton 4354 (3 lines)), who can be seen in London by appointment.

BOWDEN HOUSE

HARROW-ON-THE-HILL, MIDDLESEX

Established in 1911 Tel.: BYRon 1011 & 4772

(Incorporated Association not carried on for profit)

A private clinic for the treatment of the neuroses and nervous disorders by psychotherapy and all modern physical therapies.

Apply : MEDICAL DIRECTOR

HEIGHAM HALL, NORWICH

PRIVATE MENTAL HOME for Nervous and Mental illness. All types of treatment carried out. Accommodation for Alcoholics and Addicts available. Special Geriatric Unit now open. Fees from 7 gns. per week upwards according to requirements.

Apply to Dr. J. A. SMALL Telephone: Norwich 20080

THE MEDICAL PROTECTION SOCIETY LIMITED

Over 60 years' experience in medical defence and protection

Complete Indemnity granted to members in cases undertaken on their behalf

ANNUAL SUBSCRIPTION: £1 for first three years for newly qualified entrants and £2 thereafter

Full particulars from the Secretary (Dr. Alistair French), **Victory House, Leicester Sq., W.C.2.** Gerrard 4553 and 4814

Vacancies

ACADEMIC AND EDUCATIONAL SECTION *Page* 41

ANÆSTHETICS
St. Mary's, W.2. Sr. H.O. 45
Canterbury & Isle of Thanet H.M.C. Cons. or Sr. H.M.O... 42
Derby. Derbyshire Royal Infy. Reg. 47
Doncaster Royal Infy. Sr. H.O. .. 47
East Anglian R.H.B. P.-t. Cons. .. 42
Harefield, Middx. Sr. H.O. 48
Hemel Hempstead. West Herts. Reg. 47
Isleworth. West Middlesex. Sr. Reg. 48
Kettering Gen. Sr. H.O. 48
Leeds R.H.B. Locum Regs. 48
Manchester. N. Manchester H.M.C. Sr. H.O. 49
Norwich. Lowestoft & Great Yarmouth H.M.C. Sr. H.O. 50
Nuneaton. Manor. Sr. H.O. 50
Plymouth. South Devon & East Cornwall Gen. Hosp. Grp. Jr. H.M.O. 50
Reading. Royal Berks. Sr. H.O. .. 50
Scotland. Western R.H.B. Sr. Reg... 51
Sedgefield Gen. Sr. H.O. 51
Taplow. Canadian Red Cross Mem. Sr. H.O. 52
Taunton & Somerset. Sr. H.O. .. 53
Winchester. Royal Hampshire County. H.O. 54
St. John's, Newfoundland, Canada. Gen. Res. Anæsthetist 55

CASUALTY
Central Middlesex, N.W.10. Sr. H.O. 43
Connaught, E.17. Sr. H.O. 43
Royal Free, W.C.1. Sr. H.O. .. 44
Royal Northern, N.7. Sr. H.O. .. 44
Ashton-under-Lyne Gen. Jr. H.M.O. 45
Brighton, Royal Sussex County. H.O.'s 46
Brighton. Royal Sussex County. Jr. H.M.O. 46
Chertsey. St. Peter.'s. Sr. H.O. .. 47
Colchester Group H.M.C. Sr. H.O. . 47
Coventry & Warwickshire. Jr. H.M.O. 47
Dunfermline & West Fife. Jr. H.M.O. 49
Kettering & Dist. Gen. Sr. H.O. .. 48
Kingston, Surrey. Sr. H.O. 48
Newcastle R.H.B. Sr. Cas. O.'s .. 42
Oxford United Hosps. H.O. .. 50
Reading & Dist. H.M.C. Sr. H.O. .. 50
Shrewsbury. Royal Salop Infy. Sr. H.O. 51
Southampton. Royal South Hants. Sr. H.O. 52
Taunton & Somerset. Sr. H.O. .. 53
Watford Peace Mem. Sr. H.O. .. 53
West Indies. University College Hosp. Reg. or Sr. Reg. 55

CHEST AND TUBERCULOSIS
London Chest, E.2. Reg. 44
Plaistow, E.13. H.O. 44
Ipswich. Foxhall. Sr. H.O. 48
Leicester. Isolation Hosp. Chest Unit. Reg. 49
Newcastle upon Tyne. Walker Gate. Sr. H.O. 49
Salford. Ladywell. Jr. H.M.O. .. 51
Wakefield. Pinderfields Gen. Sr. H.O. 53
Wakefield. Pinderfields Gen. Jr. H.M.O. 53
Woodford Green. Harts. Sr. H.O. .. 54

DERMATOLOGY
Sheffield United Hosps. Reg. or Sr. H.O. 51

EAR, NOSE, AND THROAT
Royal Free Hosp. Group. Cons. .. 42
St. James', S.W.12. Reg. 44
Colchester Group H.M.C. Sr. H.O. .. 47
Edgware Gen. Sr. H.O. 47
Kingston-on-Thames. Sr. H.O. .. 48
Shrewsbury. Eye, Ear & Throat. Sr. H.O. 52
Swansea. Sr. H.O. 52

GERIATRICS
St. Matthew's, N.1. Sr. H.O... .. 45
Blackburn & Dist. H.M.C. Jr. H.M.O. 46
Bradford A & B H.M.C.'s. H.O. .. 46
Halifax. St. John's. Sr. H.O... .. 48
Oxford R.H.B. Reg. 50
Reading & Dist. H.M.C. Sr. H.O... 50
Rochford. General. Sr. H.O... .. 51

HÆMATOLOGY
Birmingham R.H.B. P.-t. Med. Pract.'s 45
Newcastle R.H.B. Jr. H.M.O. .. 49

INFECTIOUS DISEASES
Ipswich. St. Helen's. H.O... .. 48
Leeds. Seacroft. Sr. H.O. 48

MEDICINE
Charing Cross, W.C.2. Pre-reg. H.O.'s 43
King Edward Mem., W. H.O. .. 43
Metropolitan, E.8. H.O.'s 44
North West Met. R.H.B. P.-t. Cons. 42
Royal Free Hosp. Group, W.C.1. Sr. Reg. & Reg. 44
Royal Northern, N.7. H.O... .. 44
St. Mary's, W.2. Reg. & H.O. .. 44
St. Thomas's, S.E.1. Sr. Reg. .. 45
Wanstead, E.11. H.O. 45
Barnstaple. North Devon Infy. Pre-reg. H.O. 45
Chelmsford & Essex. Pre-reg. H.O... 47
Colchester Group H.M.C. Sr. H.O. .. 47
Derby. City. Sr. H.O. 47
East Anglian R.H.B. Reg. 47
Edgware Gen. H.O.'s 47
Edgware Gen. H.O. 47
Gravesend & North Kent. H.O. .. 47
Huntingdon County. H.O. 48
Leeds R.H.B. Reg. 49
Leeds R.H.B. P.-t. Cons. 42
Leeds R.H.B. Locum Regs... .. 48
Mundesley. Norfolk. Sr. H.O. .. 49
Newcastle United Hosps. Reg. .. 50
Plymouth. South Devon & East Cornwall Hosp. Pre-reg. H.O.'s.. 50
Poole Gen. Pre-reg. H.O. 50
Reading Area Dept. of Med. H.O.'s 51
Richmond, Surrey. Royal. Pre-reg. H.O. 51
Romford. Oldchurch. H.O... .. 51
Romford. Victoria. H.O. 51
Scotland. Western R.H.B. Sr. Reg... 51
Shoreham-by-Sea. Southlands. H.O. 51
Shrewsbury. Royal Salop Infy./Copthorne. H.O. 51
Southend. Gen. Pre-reg. H.O. .. 52
St. Albans City. Reg. 52
St. Albans City. H.O. 52
Stirling & Clackmannan Hosps. B.o.M. Sr. H.O.'s 52
Sunderland Area H.M.C. Sr. H.O. or H.O. 52
Torquay. Torbay. Pre-reg. H.O. .. 52
Welsh Regional Bureau. Pre-reg. H.O.'s 53
Weston-super-Mare. Gen. Pre-reg. H.O. 54

(Continued overleaf)

Winchester. Royal Hampshire County. Pre-reg. H.O. 54
York. County. Locum H.O. .. 54
York Military (Civilian Wing). Sr. H.O. 54
Cork. South Charitable Infy. & County Hosp. Reg. 54

NEUROLOGY
West End Hosp. for Neurology & Neurosurgery, W.1. Sr. H.O. .. 45
Sheffield United Hosps. Reg. or Sr. H.O. 51
U.S.A. Pennsylvania. First Assistant 43

OBSTETRICS AND GYNÆCOLOGY
City of London Maternity, N.4. H.O. 43
Forest Gate, E.7. Sr. H.O. 43
Highlands Gen., N.21. H.O. .. 43
Royal Free Hosp. Group. Regs. .. 44
Thorpe Coombe Matv., E.17. Sr. H.O. 44
Wanstead, E.11. H.O. 45
Bedford Gen. H.O. 45
Birmingham. Marston Green Maty. H.O. 45
Bishop Auckland. Gen. H.O. .. 46
Bolton Dist. Gen. H.O. 46
Brighton. New Sussex Hosp. for Women & Sussex Maty. H.O. .. 46
Bromsgrove General. H.O. 46
Bury & Rossendale H.M.C. Sr. H.O. 46
Hereford. County. Pre-reg. H.O. .. 48
Leamington. Warneford. H.O. .. 48
Oxford R.H.B. Reg. 50
Reading Combined Hosps. H.O. .. 50
St. Albans City. Locum Reg. .. 52
Stoke-on-Trent. Groundslow. H.O. 52
Stoke-on-Trent. City Gen. Locum Sr. Reg. 52
Taplow. Canadian Red Cross Mem. Pre-reg. H.O. 52
Tunbridge Wells. Pembury. Sr. H.O. 53
Welsh Regional Bureau. Pre-reg. H.O.'s 53
Winchester. Royal Hampshire County. H.O. 54

OPHTHALMOLOGY
Birmingham & Midland Eye. H.O. 46
Leeds R.H.B. Locum Sr. Reg. .. 49
Manchester United Hosps. Reg. .. 49
Newcastle United Hosps. Sr. H.O. or H.O. 50
Oxford R.H.B. Cons. 43
Swansea. Sr. H.O. 52
Wolverhampton & Midland Counties Eye Infy. Sr. H.O. 54

ORTHODONTICS
Liverpool United Hosps. & Liverpool R.H.B. Cons. 42

ORTHOPÆDICS
Highlands Gen., N.21. Sr. H.O. .. 43
King's College, S.E.5. Sr. Reg. .. 44
Royal Free, W.C.1, & Heatherwood Orthopædic, Ascot. Sr. Reg. .. 44
Royal Free, W.C.1, & Heatherwood Orthopædic, Ascot Reg. 44
St. James', S.W.12. Sr. H.O. .. 44
Birmingham R.H.B. Regs. 45
Bournemouth. Royal Victoria. Sr. H.O.'s 46
Bradford Royal Infy. H.O. 46
Brighton Gen. Pre-reg. H.O. .. 46
Burton-on-Trent Gen. Pre-reg. H.O. 46
Isleworth. West Middlesex. H.O. .. 48
Leeds R.H.B. Locum Regs. .. 48
Leeds R.H.B. Regs. 49
Leeds. Woodlands Orthopædic. Sr. H.O. 48
Manchester R.H.B. Jr. H.M.O. .. 49
Manchester. Withington. Sr. H.O. .. 49
North West Met. R.H.B. P.-t. Cons. 42
Rochester. St. Bartholomew's. Sr. H.O. 51
Romford. Oldchurch. H.O. .. 51
Rotherham. Reg. 51
Sheffield. King Edward VII Orth. Sr. H.O. 51
Shrewsbury. Royal Salop Infy. Sr. H.O. 51
Southampton. Royal South Hants. H.O. 51
South West Met. R.H.B. Locum Cons., Sr. H.M.O., or Sr. Reg. 52
Swansea. Sr. H.O. 43
Tilbury & Riverside Gen. (Orsett Branch). H.O. 52
Welsh Regional Bureau. Pre-reg. H.O.'s 52
Welsh R.H.B. Locum Cons. .. 53
Wigan. Royal Albert Edward Infy. Sr. H.O. 43
Worcester Royal Infy. H.O. .. 54

PÆDIATRICS
Price of Wales's Gen., N.15. H.O. .. 44
Whipps Cross, E.11. H.O. 45
Ashton-under-Lyne Gen. Sr. H.O. .. 45
Birmingham United Hosps. Sr. H.O. 46
Leeds United Hosps. Sr. H.O. .. 48
St. Albans City. H.O. 52
Welsh Regional Bureau. Pre-reg. H.O.'s 53
Welsh R.H.B. Reg. 53
Ibadan. University College. Sr. Reg. 54

PATHOLOGY
Dulwich, S.E.22. Sr. H.O. 43
Lambeth, S.E.11. Sr. H.O. 44
Beverley. Westwood. Sr. H.O. .. 45
Birmingham United Hosps. Sr. Reg. 46
Canterbury. Kent & Canterbury. Sr. H.O. 46
East Anglian R.H.B. Sr. H.M.O. .. 42
Hemel Hempstead. St. Paul's & West Herts. Reg. 48
Liverpool R.H.B. Sr. H.M.O. .. 42
Manchester. Withington. Sr. H.O. .. 49
Newcastle R.H.B. Sr. H.M.O. .. 42
Shrewsbury. Royal Salop Infy. Copthorne. Sr. H.O. 51
Watford. Peace Mem. Reg. 53
Woking & Chertsey Group Lab. Sr. H.O. 54
Ibadan. Nigeria University College. Reg. 55

PHYSICAL MEDICINE
Camberwell H.M.C. P.-t. Clin. Assts. 43
Royal Free Hosp., W.C.1 & Whittington, N.19. Reg. 44

PLASTIC SURGERY
Welsh R.H.B. Reg. 53

PSYCHIATRY
Abergavenny. Pen-y-Val & Maindiff Court. Jr. H.M.O. 45
Birmingham. All Saints'. Reg. .. 45
Cheddleton. St. Edward's. Jr. H.M.O. 47
Chesterfield H.M.C. Jr. H.M.O. .. 47
Leeds R.H.B. Sr. H.M.O.'s 42
Leeds R.H.B. Regs. 49
Leeds R.H.B. Locum Regs. 48
Leeds R.H.B. Locum Sr. H.M.O. .. 42
Leicester Towers. Sr. Reg. 49
Newcastle R.H.B. Locum Sr. Reg. .. 49
Newcastle R.H.B. Locum Reg. .. 49
Newcastle R.H.B. Cons. 42
North West Met. R.H.B. P.-t. Sr. H.M.O. 42
Paisley. Riccartsbar. Jr. H.M.O. .. 50
Sheffield R.H.B. Sr. H.M.O.'s .. 43
Southall. St. Bernard's Hosp. for Nervous & Mental Disorders. Sr. H.O. 51
St. Albans. Napsbury Mental. Sr. H.O. 52
Sutton, Surrey. Banstead. P.-t Sr. H.M.O. 43
Welsh R.H.B. Cons. 43
Welsh R.H.B. Reg. 53
Wickford. Runwell. Sr. H.O. .. 54
York. Clifton. Jr. H.M.O. 54

RADIOLOGY
St. Thomas's, S.E.1. Sr. H.M.O. .. 42
Eastman Dental Hosp. & Inst. of Dental Surgery. P.-t. Cons. .. 42
Blackpool Victoria. Reg. 46

RADIOTHERAPY
Hammersmith Hosp. & P.G. Med. School, W.12. H.O.'s 43
Middlesex, W.1. Reg. 44
Manchester R.H.B. Cons. 42
Manchester R.H.B. Regs. 49
Welsh R.H.B. Reg. 53
Australia. Cancer Institute Board, Melbourne. Cons. 43

SURGERY
Bethnal Green, E.2. Pre-reg. H.O. .. 43
Charing Cross, W.C.2. Pre-reg. H.O.'s 43
Connaught, E.17. H.O. 43
Lambeth, S.E.11. H.O. 44
Metropolitan, E.8. H.O.'s 44
Middlesex, W.1. Reg. 44
Nelson, S.W.20. H.O. 44
North Middlesex, N.18. Locum Reg. 44
South London Hosp. for Women & Children, S.W.4. Reg. 44
St. Thomas's, S.E.1. Regs. 45
Wimbledon, S.W.20. H.O. 45
Aberystwyth. Gen. H.O. 45
Ashford, Middx. H.O. 45
Ashford, Middx. Reg. 45
Birmingham Accident. Sr. H.O. .. 45
Birmingham Accident. H.O.'s .. 45
Birmingham R.H.B. Reg. 45
Birmingham R.H.B. Regs. 45
Birmingham United Hosps. H.O.'s 46
Blackpool Victoria. Pre-reg. H.O. .. 46
Bournemouth. Royal Victoria. H.O. 46
Bradford Royal Infy. H.O.'s .. 46
Bradford. St. Luke's. H.O. .. 46
Brighton. Royal Sussex County. H.O. 46
Canterbury, Kent & Canterbury. H.O. 46
Chelmsford & Essex. Pre-reg. H.O. 47
Chelmsford. St. John's. Sr. H.O. .. 46
Derby. Derbyshire Royal Infy. Sr. H.O. 47
Derby City Hosp. Reg. 47
Dorchester. Dorset County. Pre-reg. H.O. 47
Ebbw Vale, Mon. Jr. H.M.O. .. 47
Enfield. Chase Farm. Pre-reg. H.O. 47
Epsom Dist. Pre-reg. H.O. 47
Gravesend & North Kent. H.O. .. 47
Grimsby. Scartho Road. Pre-reg. H.O. or Sr. H.O. 47
Hereford County. Pre-reg. H.O. .. 48
Hereford Gen. Pre-reg. H.O.'s & Locum Sr. H.O. 48
Hounslow, Middx. H.O. 48
Huddersfield Royal Infy. H.O.'s .. 48
Hull. Kingston Gen. H.O. 48
Ilford, King George. Pre-reg. H.O.'s 48
Ipswich & East Suffolk. H.O.'s 48
Kettering & Dist. Gen. Pre-reg. H.O. 48
Kidderminster & Dist. Gen. Pre-reg. H.O. 48
Leeds R.H.B. Regs. 49
Leeds R.H.B. Locum Regs. 48
Manchester. Booth Hall Child.'s. H.O. 49
Manchester. N. Manchester H.M.C. Pre-reg. H.O.'s 49
Manchester R.H.B. Reg. 49
Newark Gen. Jr. H.M.O. 49
Newton Abbot, Devon. Sr. H.O.'s 50
Nottingham Gen. Pre-reg. H.O. .. 50
Nuneaton. Manor. Pre-reg. H.O. .. 50
Oldham & Dist. H.M.C. Locum Sr. H.O. 50
Oxford United Hosps./R.H.B. Sr. Regs. 50
Plymouth. South Devon & East Cornwall Hosp. Pre-reg. H.O.'s. . 50
Poole Gen. Pre-reg. H.O. 50
Reading. Royal Berks. H.O.'s .. 50
Richmond, Surrey. Royal. Pre-reg. H.O. 51
Rochester. St. Bartholomew's. Pre-reg. H.O. 51
Romford. Oldchurch. H.O.'s .. 51
Scotland. Northern R.H.B. P.-t. Cons. 43
Shoreham-by-Sea. Southlands. H.O. 51
Shrewsbury. Royal Salop Infy. H.O.'s 51
Slough. Upton. Locum Sr. Reg. .. 52
Southend. Gen. Pre-reg. H.O. .. 52
Stirling & Clackmannan Hosps. B.o.M. Pre-reg. H.O. 52
Stockport Infy. Sr. H.O. 52
Stockport Infy. H.O. 52
Stockport. Stepping Hill. Pre-reg. H.O. 52
Taplow. Canadian Red Cross Mem. H.O. 52
Walsall H.M.C. Locum Sr. H.O. .. 54
Watford Hosps. Unit. H.O. 53
Welsh Regional Bureau. Pre-reg. H.O.'s 53
Welsh R.H.B. Locum Sr. H.M.O. .. 43
Welsh R.H.B. Reg. 53
Winchester. Royal Hampshire County. H.O. 54
Windsor. King Edward VII. Pre-reg. H.O. 54
Windsor. King Edward VII. H.O. .. 54
Wolverhampton. Royal. Pre-reg. H.O. 54
Worcester Royal Infy. H.O. .. 54
Workington Infy. Pre-reg. H.O. or Sr. H.O. 54
Wrexham. Maelor Gen. & War Mem. H.O.'s 54
York County Hosp. Pre-reg. H.O. 54
Cork. South Charitable Infy. & County Hosp. Reg. 54

THORACIC SURGERY
Leeds R.H.B. Reg. 49
Scotland. Eastern R.H.B. Sr. Reg. or Reg. 51
Wakefield. Pinderfields Gen. Sr. H.O. 53
Wolverhampton. Royal. Sr. H.O. .. 54

VENEREOLOGY
North West Met. R.H.B. P.-t. Cons. 42

GENERAL
Canada. Regina Gen. Jr. Rotating Internships 54
Michigan. U.S.A. Oakwood Hosp. Residency 55

PUBLIC APPOINTMENTS 55

GENERAL PRACTICE 56

MISCELLANEOUS 56

The Terms and Conditions of Service of Hospital Medical and Dental Staff apply to all N.H.S. hospital posts we advertise, unless otherwise stated. Canvassing disqualifies, but candidates may normally visit the hospital by appointment.

Academic and Educational

ROYAL COLLEGE OF PHYSICIANS OF LONDON

The next EXAMINATION for the MEMBERSHIP will commence on MONDAY, 29TH DECEMBER, 1958.

Prospective candidates are asked to note that entries accompanied by the certificates, testimonials and the examination fee of 15 guineas as required by the Bye-laws, must reach the College not later than first post on Monday, 1st December, 1958. Candidates must have been qualified for 18 months.

Candidates who propose to submit published work under the regulations are required to give 28 days' notice, and should apply in writing to the Registrar, without delay, for detailed instructions as to the procedure they should follow. Completed entries for published work must also reach the College not later than first post on Monday, 1st December.

HAROLD BOLDERO, D.M., Registrar.

12, Pall Mall East, London, S.W.1.

INSTITUTE OF ORTHOPÆDICS

PROVISIONAL PROGRAMME
COURSE ON NEUROLOGY IN ORTHOPÆDICS
13TH–15TH NOVEMBER, 1958

L = Lecture
D = Demonstration
LD = Lecture-Demonstration

Thursday, 13th November—Town Section (234, Great Portland-street, W.1)

In the Lecture Room :

LD	9.30–11.00	Cerebral Palsy (excluding treatment)	Dr. P. H. SANDIFER
	11.00	Coffee	
L/LD	11.30–12.30	Lumbar Interverte-bral Disc Lesions	Mr. P. H. NEWMAN
	12.45	Lunch (refectory)	
L/LD	1.45– 2.45	Cervical Interverte-bral Disc Lesions	Mr. H. OSMOND-CLARKE
LD	2.45– 4.15	Nerve Injuries	Mr. H. J. SEDDON
	4.15	Tea (refectory)	

Friday, 14th November—Country Section (Brockley Hill, Stanmore, Middlesex)

In the Research Block :

D	10.00–11.00	Poliomyelitis : Early Treatment	Mr. D. M. BROOKS
	11.00	Coffee	
D	11.30–12.30	Poliomyelitis : Respiratory Paralysis	Dr. A. B. KINNIER-WILSON
	12.45	Lunch	
D	2.00– 3.00	Poliomyelitis : Late Treatment	Mr. J. A. CHOLMELEY
LD	3.00– 4.00	Compression Paraplegia	Mr. R. C. CONNOLLY
	4.00	Tea	

Saturday, 15th November—Country Section (Brockley Hill, Stanmore, Middlesex)

In the Research Block :

LD	10.00–11.00	Electrodiagnosis	Dr. D. A. BREWERTON
	11.00	Coffee	
LD	11.30–12.30	Treatment of Cerebral Palsy	Mr. K. I. NISSEN

The fee for this course (including coffee, lunch, and tea) is 3 guineas.

Early application should be made to the Dean, at 234, Great Portland-street, London, W.1.

THE KETTLE MEMORIAL LECTURE

The Kettle Memorial lecture will be delivered by Dame JANET M. VAUGHAN, D.B.E., D.M., F.R.C.P., on "The Relation of Radiation Dose to Radiation Damage with Reference to Bone-seeking Isotopes" in the Physiology Lecture Theatre, St. Bartholomew's Hospital Medical College, Charterhouse-square, London, E.C.1, on THURSDAY, 27TH NOVEMBER, 1958, at 5 P.M.

Medical practitioners and medical undergraduates are invited to attend.

UNIVERSITY OF LONDON INSTITUTE OF EDUCATION

DIPLOMA IN THE CONTENT AND METHODS OF HEALTH EDUCATION

An ADVANCED COURSE for full-time students occupying 1 university year is open to qualified teachers, training college lecturers, medical practitioners, qualified nurses and others who are interested in the field of Health Education.

Candidates should have had experience in their own field and possess sufficient scientific background to satisfy the Institute that they can profit from the course.

The course is organised by the Institute of Education with the cooperation of the London School of Hygiene and Tropical Medicine and of the Central Council for Health Education.

Further particulars may be obtained from Miss W. M. WARDEN, Senior Lecturer in Health Education, Institute of Education, Malet-street, W.C.1.

MAKERERE COLLEGE
THE UNIVERSITY COLLEGE OF EAST AFRICA

Applications are invited for (*a*) READERSHIP or (*b*) SENIOR LECTURESHIP IN CLINICAL PHYSIOLOGY, tenable from July, 1959. Salary scales: (*a*) £2256–£72–£2400 p.a., (*b*) £2085–£72–£2301 p.a., point of entry determined by qualifications and experience. F.S.S.U. Child allowance £50 p.a. per child (maximum £150 p.a.). Passages for appointee and family (up to 4 adult passages) on appointment, termination and leave (3 months every 21 months). Rent according to quarters provided, £45–£84 p.a. (including basic furniture).

Applications (6 copies), naming 3 referees, by 1st January, 1959, to Secretary, Inter-University Council for Higher Education Overseas, 29, Woburn-square, London, W.C.1, from whom further particulars may be obtained.

UNIVERSITY COLLEGE OF SOUTH WALES AND MONMOUTHSHIRE
UNIVERSITY OF WALES

RESEARCH FELLOWSHIP IN PÆDIATRIC PHYSIOLOGY

Applications are invited for a Research Fellowship to be established in the Department of Physiology for the study of problems relating to the physiology of infancy and childhood. The Fellow appointed will be encouraged to proceed to a higher University degree and will be given considerable freedom to choose the subject to be investigated.

The Fellowship, which is tenable for a maximum of 3 years, is valued at £700 p.a. with increments of £25 for each of the second and third years upon completion of a satisfactory probationary period. Duties are to commence on 1st January, 1959, or as soon after as possible.

Applications (6 copies) (containing the names of 2 referees), should be sent to the Registrar, University College of South Wales and Monmouthshire, Cathays Park, Cardiff, by 30th November, 1958.

UNIVERSITY OF EDINBURGH
EDINBURGH POST-GRADUATE BOARD FOR MEDICINE

Applications are invited for the post of DIRECTOR OF STUDIES which will shortly become vacant. The qualities desirable are senior clinical and administrative experience and a knowledge and understanding of the problems of Commonwealth postgraduate students. The full-time salary is £2000, with F.S.S.U. and family allowance where applicable.

Particulars of the duties, which include the organisation of numerous postgraduate courses and activities, may be obtained from the Secretary to the University, Old College, South Bridge, Edinburgh. The closing date for applications is 31st December, 1958.

GUY'S HOSPITAL MEDICAL SCHOOL, S.E.1. Applications are invited for the following appointments in the Department of Bacteriology:—

(*a*) JUNIOR LECTURER or LECTURER. Salary range £900–£1750.

(*b*) LECTURER or SENIOR LECTURER. Salary range £1100–£1950.

Salaries will depend on qualifications and experience, with superannuation and family allowance. Candidates should have a medical or scientific degree and an interest in a fundamental approach to microbiological problems.

Applications should be submitted, on a form obtainable from the Dean, not later than 14th November, 1958.

BRADFORD INSTITUTE OF TECHNOLOGY (Principal : E. G. Edwards, PH.D., B.SC., F.R.I.C.). Applications are invited for the following new posts :—

CHIEF TECHNICIAN in the Departments of Pharmacy and Biological Sciences.
Salary scale £725–£30–£845.
SENIOR TECHNICIAN IN PHARMACEUTICAL CHEMISTRY.
SENIOR TECHNICIAN IN PHARMACOLOGY AND PHYSIOLOGY.
SENIOR TECHNICIAN IN PHARMACEUTICS.
Salary scale £625–£20–£745 (with efficiency bar at £685).

Candidates should possess a City and Guilds Laboratory Technicians' Certificate or hold a qualification of the Institute of Medical Laboratory Technologists and have previous suitable experience.

Further details and forms of application may be obtained from the Principal, Bradford Institute of Technology, Bradford, 7.

W. H. LEATHEM, Clerk to the Governors.

KING'S COLLEGE, UNIVERSITY OF DURHAM, and the UNITED NEWCASTLE UPON TYNE HOSPITALS. Applications are invited for the appointment of FIRST ASSISTANT in the Department of Obstetrics and Gynæcology. The appointment is for 1 year in the first instance, renewable annually to a maximum of not more than 3 years. The commencing salary will be within the range of £1400–£1900. Candidates should possess a higher qualification in midwifery and gynæcology, should have had considerable experience in the specialty and should be prepared to participate in research projects. The successful applicant will hold his appointment jointly in King's College and in the United Newcastle upon Tyne Hospitals and will work in rotation in the Department of Gynæcology in the Royal Victoria Infirmary and in the Princess Mary Maternity Hospital.

Further particulars may be obtained from the undersigned, to whom applications (12 copies), together with the names of 3 referees, should be sent not later than a fortnight after the publication of this advertisement.

G. R. HANSON, Registrar of King's College.

THE UNIVERSITY OF LEEDS. Department of Pathology. Applications are invited from candidates with a registered medical qualification for appointment as ASSISTANT LECTURER IN PATHOLOGY at a salary on the scale £900–£100–£1100 a year, according to age, qualifications and experience. The person appointed will be required to assist in the routine work of the Department of Pathology (which includes the hæmatology of the General Infirmary at Leeds) but will be expected also to take part in some research.

Applications (3 copies), stating date of birth, qualifications and experience, together with the names of 3 referees, should reach the Registrar, The University, Leeds, 2 (from whom further particulars may be obtained), not later than 1st December, 1958.

THE UNIVERSITY OF LEEDS. Department of Surgery. Applications are invited for appointment to a TEMPORARY LECTURESHIP IN THORACIC SURGERY at a salary within the range £1200–£1900 a year, for 1 year in the first instance, renewable up to a total of 3 years.

Applications (3 copies), stating date of birth, qualifications and experience, together with the names of 3 referees, should reach the Registrar, The University, Leeds, 2 (from whom further particulars may be obtained), not later than 24th November, 1958.

AUSTRALIA. UNIVERSITY OF QUEENSLAND. Applications are invited for the position of PROFESSOR OF PHYSIOLOGY, with salary of £A3500 p.a.

Further particulars and application forms are obtainable from the Secretary, Association of Universities of the British Commonwealth, 36, Gordon-square, London, W.C.1. Applications close, in Australia and London, on 15th December, 1958.

Hospital Services: Senior Appointments

EASTMAN DENTAL HOSPITAL AND INSTITUTE OF DENTAL SURGERY (UNIVERSITY OF LONDON), Gray's Inn-road, London, W.C.1. Applications are invited for the part-time appointment of CONSULTANT RADIOLOGIST on the basis of 5 sessions a week. The appointment is in accordance with the terms and conditions of service of hospital medical and dental staff.

Applications, including the names of 2 referees, should be sent before 24th November, 1958, to the Director, from whom further particulars may be obtained.

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD.

1. CONSULTANT ORTHOPÆDIC SURGEON, 3 half-days a week, Harefield and Northwood Group of hospitals. Duties mainly at Mount Vernon Hospital, Northwood (551 Beds).

Applications before 1st December, 1958.

2. CONSULTANT PHYSICIAN, 3 half-days a week, Royal Northern Hospital, Holloway, N.7 (277 Beds).

3. CONSULTANT VENEREOLOGIST, 5 half-days a week (including some evening sessions), Central Middlesex Hospital, Park Royal, N.W.10 (726 Beds).

Applications before 10th December, 1958.

Hospitals may be visited by direct appointment.

4. CHILD PSYCHIATRIST (Senior Hospital Medical Officer grade), 6 half-days a week, Child Guidance Clinics, 58, Hampton-road, Twickenham, and The Grange, Gresham-road, Staines. Clinics may be visited by arrangement with the Area Health Officer, Elmfield House, High-street, Teddington.

Applications before 3rd December, 1958.

Application forms obtainable from and returnable to Secretary, North West Metropolitan Regional Hospital Board, 40, East-bourne-terrace, W.2.

ROYAL FREE HOSPITAL GROUP. Applications are invited from registered medical practitioners for the appointment of CONSULTANT SURGEON to the E.N.T. Department (2 sessions). Applicants must be Fellows of the Royal College of Surgeons (England).

Applications, giving details of experience and accompanied by the names of 3 referees, should be sent to the Secretary to the Board of Governors, The Royal Free Hospital, Gray's Inn-road, W.C.1, not later than 21st November, 1958.

ST. THOMAS'S HOSPITAL, London, S.E.1. Assistant RADIOLOGIST to the X-ray Diagnostic Department. Whole-time. Salary £1653 15s.–£2126 5s. p.a.

Applications (9 copies), naming 2 referees, to the Clerk of the Govenors by 10th November, 1958.

CANTERBURY AND ISLE OF THANET HOSPITAL MANAGEMENT COMMITTEES. Applications are invited for the post of ANÆSTHETIST (Consultant or Senior Hospital Medical Officer grade) for the period 26th January–3rd May, 1959, inclusive.

Applications, with full details and names of referees, to be addressed to the Group Secretary, Central Office, Nunnery Fields Hospital, Canterbury, as soon as possible.

EAST ANGLIAN REGIONAL HOSPITAL BOARD.

(1) CONSULTANT ANÆSTHETIST (maximum part-time), North Cambridgeshire Hospital Group. Duties will be mainly at the North Cambridgeshire Hospital, Wisbech and County Hospital, Doddington, and will also entail relief work in adjoining hospital groups. Candidates are invited to visit hospitals by direct arrangement with Hospital Management Committee Secretary, North Cambridgeshire Hospital, Wisbech.

(2) ASSISTANT CLINICAL PATHOLOGIST (whole-time) to hospitals in the West Suffolk area. Main laboratories at Newmarket General Hospital (338 Beds) and West Suffolk General Hospital, Bury St. Edmunds (262 Beds). Higher qualification desirable. Salary scale £1653 15s.–£2126 5s. Candidates invited to visit hospitals by direct arrangement with the Consultant Pathologist at each hospital.

Applications (8 copies), stating age, experience, and the names of 3 referees, to Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, by 24th November, 1958.

MANCHESTER REGIONAL HOSPITAL BOARD. Whole-time or maximum part-time CONSULTANT RADIOTHERAPIST, Christie Hospital and Holt Radium Institute, Manchester. F.F.R. essential, other higher medical or surgical qualifications desirable.

Application forms from the Senior Administrative Medical Officer to the Board, Manchester, 8, to be returned by 5th December, 1958.

LEEDS REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of Locum ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer grade) for duties at Stanley Royd Hospital, Wakefield (1976 Beds).

Applications, giving full details of age, qualifications and previous appointments (with dates), together with the names and addresses of 3 referees, should be addressed to the Secretary, Park Parade, Harrogate, by 12th November, 1958.

LEEDS REGIONAL HOSPITAL BOARD. Maximum Part-time CONSULTANT in General Medicine and Geriatrics (approximately 45% of the duties) for the Bingley, Keighley, Skipton and Settle Areas. Person appointed to reside in or near Keighley.

Applications (12 copies), stating age, qualifications, and details of present and previous appointments with dates, and names and addresses of 3 referees, to the Secretary, Park Parade, Harrogate, by 18th November, 1958.

LEEDS REGIONAL HOSPITAL BOARD. Whole-time ASSISTANT PSYCHIATRISTS (Senior Hospital Medical Officer grade).

Menston Hospital, near Leeds (2500 Beds), and associated general hospitals. Married and single accommodation available.

Storthes Hall Hospital (2680 Beds), Kirkburton, near Huddersfield, and associated general hospitals. Resident or non-resident. Large modern flat available if required. Accommodation also available for single person.

Candidates for these Senior Hospital Medical Officer posts should normally hold a D.P.M., but applications will also be considered from candidates without previous experience in psychiatry who hold a higher qualification and have had wide experience in general medicine in the Senior Registrar grade and who intend to obtain a D.P.M. and specialise in psychiatry.

Applications (12 copies), stating age, qualifications, and details of present and previous appointments, with dates, and names and addresses of 3 referees, to the Secretary, Park Parade, Harrogate, by 18th November, 1958.

LIVERPOOL REGIONAL HOSPITAL BOARD. BIRKENHEAD GROUP. Applications are invited for the post of Whole-time ASSISTANT PATHOLOGIST (Senior Hospital Medical Officer) in the above Group, with duties mainly at St. Catherine's Hospital. Applicants should have general all-round experience in clinical pathology. The possession of a higher qualification in pathology will be considered an advantage.

Forms of application from Dr. T. Lloyd Hughes, Senior Administrative Medical Officer, Liverpool Regional Hospital Board, 55, Castle-street, Liverpool, 2, to be returned not later than 22nd November, 1958.

VINCENT COLLINGE, Secretary to the Board.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. LIVERPOOL REGIONAL HOSPITAL BOARD. Applications are invited for appointment as CONSULTANT ORTHODONTIST for duty at the Liverpool Dental Hospital and the Royal Liverpool Children's Hospital in The United Liverpool Hospitals, where the post will be of Junior status, and at Alder Hey Children's Hospital. The post will be mainly concerned with the expansion of cleft palate services and may be held on a full-time or maximum part-time basis. 4 of the sessions will be devoted to Alder Hey Children's Hospital and the remaining sessions to The United Liverpool Hospitals. Candidates must possess a registrable qualification and a higher qualification in dentistry, and should have had appropriate experience.

Applications (1 copy only) giving full particulars of age, qualifications, &c., and details of present and previous appointments, together with the names of 3 persons to whom reference may be made, should reach the Secretary, The United Liverpool Hospitals, 80, Rodney-street, Liverpool, 1, by the 3rd December, 1958.

NEWCASTLE REGIONAL HOSPITAL BOARD. Senior CASUALTY OFFICER, whole-time, for the Sunderland Group of hospitals, mainly at Sunderland Royal Infirmary (300 Beds). Appointment for a period not exceeding 4 years. Duties, subject to supervision of one of the Senior General Surgeons, to organise and handle work of Casualty Department. Salary within range of £1653 15s.–£2126 5s. or £1548 15s.–£2126 5s. p.a., according to age. Applicants may visit the department by arrangement with Mr. T. G. LOWDEN, F.R.C.S., Royal Infirmary, Sunderland.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 28 days.

NEWCASTLE REGIONAL HOSPITAL BOARD. Senior CASUALTY OFFICER, whole-time, for South Tees-side Group of hospitals. This is a new appointment in connection with the new Accident and Orthopædic Wing (169 Beds) which is to be opened early in 1959. The duties include both outpatient and inpatient work and will be under the general supervision of the consultant surgical staff; the Senior Casualty Officer will work as a member of the team dealing with orthopædic and accident surgery. Appointment for a period not exceeding 4 years. Salary within range of £1653 15s.–£2126 5s. or £1548 15s.–£2126 5s p.a., according to age.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 28 days.

NEWCASTLE REGIONAL HOSPITAL BOARD. Assistant PATHOLOGIST (Senior Hospital Medical Officer), whole-time or maximum part-time, for the Sunderland Group of hospitals—main hospitals Royal Infirmary (300 Beds), General (461 Beds), Ryhope General (282 Beds). There are 1978 Beds in the group serving population of 363,000. Consultant staff of 3.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 28 days.

NEWCASTLE REGIONAL HOSPITAL BOARD. Consultant PSYCHIATRIST AND DEPUTY MEDICAL SUPERINTENDENT, whole-time, for St. Nicholas Hospital, Gosforth, Newcastle upon Tyne, 3 (1193 Beds). The Hospital contains a fully-equipped neurosurgical theatre and an active Electroencephalographic Department; a modern admission unit and 2 convalescent villas on a detached site have recently been added. The areas served by the Hospital include Newcastle County Borough and parts of the Counties of Northumberland and Durham. Candidates should have had wide experience in intra- and extra-mural psychiatry and be competent to take clinical charge, subject to the general administrative control of the Medical Superintendent, of a section of the Hospital and to participate in the work of the associated outpatient clinics. Members of the clinical team, act as Associate Physicians to the Department of Psychological Medicine, Newcastle General Hospital. House available on a temporary basis; new house to be provided in 1959–60. Further particulars from Regional Psychiatrist.

Applications to the Regional Psychiatrist, Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 28 days.

OXFORD REGIONAL HOSPITAL BOARD. Consultant OPHTHALMOLOGIST (whole-time or maximum part-time) to the Northampton/Kettering Area Department of Ophthalmology. Service is based on the new ophthalmic ward (32 Beds) at Northampton General Hospital.

Applications, giving details of qualifications, experience, and the names of 3 referees, should reach the Secretary, 43, Banbury-road, Oxford, by 22nd November, 1958.

SCOTLAND. NORTHERN REGIONAL HOSPITAL BOARD. Applications are invited for the post of Part-time CONSULTANT in General Surgery and SURGEON-SUPERINTENDENT, Belford Hospital, Fort William (9 notional half-days). A suitable house is available.

Schedules of application and further particulars may be obtained from the undersigned, with whom applications should be lodged, by 1st December, 1958.

A. M. FRASER, M.D.,
Secretary and Administrative Medical Officer.

Office of the Northern Regional Hospital Board,
Reay House, 17, Old Edinburgh-road, Inverness.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time SENIOR ASSISTANT PSYCHIATRIST required to be designated Deputy Medical Superintendent of Glenfrith Hospital for Mental Defectives, Leicester. A house is available. Salary £1653 15s.–£52 10s.–£2126 5s. p.a.

Application forms and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 22nd November, 1958.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time SENIOR ASSISTANT PSYCHIATRIST required at the Pastures Hospital, Mickleover, near Derby. Salary scale £1653 15s.–£52 10s.–£2126 5s. p.a.

Application forms and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 22nd November, 1958.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires a Locum Tenens ORTHOPÆDIC SURGEON of Consultant, Senior Hospital Medical Officer or Senior Registrar status, for 9 sessions weekly, for the Southampton and Winchester Groups of hospitals immediately for approximately 2 months. The main duties will be at the Royal South Hants Hospital, Southampton, and the Royal Hampshire County Hospital, Winchester. Candidates should preferably have had experience as a Senior Registrar.

Applications (2 copies), stating age, qualifications and experience, and giving the names and addresses of 3 referees, to the Area Secretary, Highcroft, Romsey-road, Winchester, by 10th November, 1958.

SUTTON, SURREY. BANSTEAD HOSPITAL. (2400 Beds.) Applications are invited for the post of SENIOR HOSPITAL MEDICAL OFFICER (6 half-day sessions per week), for a new Mother and Baby Unit to be developed at the above Hospital. This Unit will continue a research programme into the problems of mothers suffering from a schizophrenic illness. Applicants should have experience of psychoanalysis as well as general psychiatry. Previous experience with this type of problem is essential.

Candidates should apply to the Secretary for forms of application, which should be completed and returned within 14 days from the appearance of this advertisement. Candidates may visit the Hospital by arrangement with the Physician-Superintendent.

WELSH REGIONAL HOSPITAL BOARD. Whole-time CONSULTANT PSYCHIATRIST, Morgannwg Hospital, Bridgend (2359 Beds). Applicants must have had wide experience in psychiatry, hold a Diploma in Psychological Medicine, be competent to take clinical responsibility and to participate in the work of the Associated Outpatient Clinics and Domiciliary Consultant Service in the area served by the Hospital. Electroencephalographic experience will be an additional advantage. Married accommodation available if required.

Applications (12 copies), naming 3 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 21 dyas.

WELSH REGIONAL HOSPITAL BOARD. Whole-time Locum Tenens CONSULTANT ORTHOPÆDIC AND TRAUMATIC SURGEON required, Clwyd and Deeside Hospital Management Committee area, immediately.

Applications, naming 2 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff.

WELSH REGIONAL HOSPITAL BOARD. Whole-time Locum Tenens SENIOR HOSPITAL MEDICAL OFFICER (traumatic and orthopædic surgery) required, Caerphilly District Miners' Hospital, immediately for approximately 2 months.

Applications, naming 2 referees, to Senior Administrative Medical Officer, Temple of Peace and Health, Cathays Park, Cardiff.

AUSTRALIA. CANCER INSTITUTE BOARD, 483, Little Lonsdale-street, MELBOURNE, AUSTRALIA. Applications are invited from suitable qualified medical practitioners for the position of CONSULTANT RADIOTHERAPIST. In addition to clinical duties at Melbourne, the appointee will be required to conduct consultative peripheral clinics within the State of Victoria. The Institute has modern equipment for radiotherapy, including a 4 MeV. Linear Accelerator and other well-appointed services for treatment of inpatients and outpatients (22,700 attendances annually). There are facilities for research in the clinical sphere, medical physics and pathology. The full-time salary will be within the range of £A3306–£A3756 p.a. Consultant Officers are entitled to limited private practice within the Institute. Other terms of the appointment include superannuation, long service leave, recreational and sick leave entitlements. The position is non-resident. An appointee from overseas will be granted first-class fares for himself and family, also an allowance of £200 sterling for the transport of furniture and personal effects.

Further information is available from the undersigned, with whom applications close on 30th November, 1958.

R. K. CHURCHES, Manager and Secretary.

U.S.A. PENNSYLVANIA HOSPITAL, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA. NEUROLOGICAL FIRST ASSISTANT required at the Neurological Unit of the above Hospital for a period of 1 or more years. Experience of electroencephalography and neurophysiology advantageous but not essential. Salary $8000 p.a.

Applications, including full biographical details together with reprints of original work, should reach Dr. F. A. ELLIOTT, 56, Wimpole-street, W.1, before 15th December, 1958.

Hospital Services: Junior Appointments

BETHNAL GREEN HOSPITAL, Cambridge Heath-road, London, E.2. HOUSE SURGEON, pre-registration post. Vacant 1st December, 1958.

Apply, stating experience, with copies of 2 testimonials, to Hospital Secretary.

CAMBERWELL HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for appointment to paid CLINICAL ASSISTANTSHIPS for 2 sessions a week in the Department of Physical Medicine with this Group, which comprises Dulwich St. Francis' and St. Giles' Hospitals, and the Rheumatism Clinic, Peckham Rye.

Applications, giving details of qualifications and experience, should be sent to the Group Secretary, Camberwell Hospital Management Committee, Dulwich Hospital, S.E.22, to reach him not later than 14th November, 1958.

CENTRAL MIDDLESEX HOSPITAL, Park Royal, N.W.10. SENIOR HOUSE OFFICER required for Casualty Department. Successful candidate will work under supervision of orthopædic and traumatic specialist. Post now vacant.

Applications, with 2 testimonials or names of 2 referees, to Medical Director by 8th November.

CHARING CROSS HOSPITAL, W.C.2. Applications are invited for the following pre-registration appointments, tenable for 6 months from 1st January, 1959:—

(*a*) **Harrow Hospital**
1 HOUSE PHYSICIAN.
2 HOUSE SURGEONS.
(*b*) **Wembley Hospital**
1 HOUSE PHYSICIAN.
3 HOUSE SURGEONS.

Application forms to be returned to the undersigned by 17th November, 1958. FRANK HART, Secretary to the Board.

CITY OF LONDON MATERNITY HOSPITAL, Hanley-road, London, N.4. OBSTETRIC HOUSE SURGEON. Recognised for M.R.C.O.G. Vacant 1st December.

Application form from Hospital Secretary, returnable by 14th November, 1958.

CONNAUGHT HOSPITAL, Walthamstow, E.17. (123 Beds.) Applications are invited for the post of SECOND CASUALTY OFFICER with duties in the Department of Orthopædic and Traumatic Surgery (Senior House Officer grade). Recognised for F.R.C.S. Salary £819 10s. p.a., less £150 p.a. for board, lodging, &c.

Applications, with full details and copies of 2 recent testimonials, should be sent immediately to Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

CONNAUGHT HOSPITAL, Walthamstow, E.17. (123 Beds.) HOUSE SURGEON required for 6 months. Recognised for F.R.C.S.

Applications, with full details and copies of 2 recent testimonials, should be sent immediately to Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

DULWICH HOSPITAL, East Dulwich-grove, S.E.22. SENIOR HOUSE OFFICER (pathology) required from 1st December, 1958. The Hospital is associated with King's College Hospital Medical School for teaching purposes.

Apply, giving age, qualifications and experience, with copy testimonials or names of 2 referees, to Group Secretary, Camberwell Hospital Management Committee, Dulwich Hospital, not later than 12th November, 1958.

FOREST GATE HOSPITAL, Forest-lane, E.7. Senior OBSTETRIC HOUSE OFFICER required for 1 year from 1st January, 1959. The appointment is recognised for training candidates for M.R.C.O.G. and D.Obst.R.C.O.G.

Applications, with names of 2 referees, to the Hospital Secretary by 12th November.

HAMMERSMITH HOSPITAL AND POSTGRADUATE MEDICAL SCHOOL, Ducane-road, London, W.12. 2 RESIDENT HOUSE SURGEONS (radiotherapy) required 1st January. These posts offer opportunities for attending general surgical postgraduate teaching.

Detailed applications, copies 2 recent testimonials, to Secretary, Board of Governors, The Hammersmith, West London and St. Mark's Hospitals, Ducane-road, London, W.12, by 8th November.

HIGHLANDS GENERAL HOSPITAL, Winchmore Hill, London, N.21. HOUSE SURGEON for Gynæcological and General Surgery.

Applications, with copies of 3 testimonials and name and address of 1 referee, to Hospital Secretary.

HIGHLANDS GENERAL HOSPITAL, Winchmore Hill, N.21. ORTHOPÆDIC HOUSE SURGEON, Senior House Officer grade. Some E.N.T. and emergency general surgery. New operating-theatre, Outpatient and Casualty Department.

Applications, with copies of 3 testimonials and name and address of 1 referee, to Hospital Secretary.

KING EDWARD MEMORIAL HOSPITAL, Ealing. House PHYSICIAN. Vacant 1st December. Preference given to persons seeking pre-registration post.

Applications, stating age, nationality, qualifications and experience, with dates, and copies of 2 recent testimonials, to Group Secretary, South West Middlesex Hospital Management Committee, West Middlesex Hospital, Isleworth, by 10th November, 1958.

KING'S COLLEGE HOSPITAL, Denmark Hill, S.E.5. Applications are invited for the post of SENIOR REGISTRAR in Orthopædics. The post is tenable from 5th January, 1959, until 30th September, 1959, in the first instance. Facilities for research are available in the new surgical unit.

Applications, together with the names of 2 referees, should be submitted to the undersigned not later than 15th November, 1958.
S. W. BARNES, House Governor.

LAMBETH HOSPITAL, Brook-drive, S.E.11. Resident HOUSE SURGEON required. Applicants may be either registered or of pre-registration status. Post recognised for F.R.C.S. Vacant 5th December, 1958. Successful candidate will be required to carry out fortnight's locum duty, commencing 21st November, 1958.

Application forms from Hospital Secretary.

LAMBETH HOSPITAL, Brook-drive, S.E.11. Lambeth GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER in Pathology for 6 months, at the Group Laboratory. Vacant now. Hospital recognised for Diploma in Pathology.

Application form from the Secretary.

LONDON CHEST HOSPITAL. Hospitals for Diseases OF THE CHEST. Applications are invited for the appointment of RESIDENT MEDICAL OFFICER. Appointment for 1 year from 1st January, 1959, and graded as Registrar.

Applications, stating date of birth, qualifications, with dates, and previous appointments held, with copies of 3 testimonials, should be sent to the undersigned not later than 13th November.
J. ROBBINS, House Governor.

London Chest Hospital, E.2.

METROPOLITAN HOSPITAL, Kingsland-road, London, E.8. (General—146 Beds.) Applications are invited for the pre-registration posts of 2 HOUSE PHYSICIANS, vacant 1st January, 1959.

Applications from provisional and fully registered candidates, stating age, nationality, qualifications and experience, with copies of 3 recent testimonials to the Hospital Secretary by 17th December, 1958.

METROPOLITAN HOSPITAL, Kingsland-road, London, E.8. (General—146 Beds.) Applications are invited for the pre-registration posts of 3 HOUSE SURGEONS, vacant 1st January, 1959.

Applications from provisional and fully registered candidates, stating age, nationality, qualifications and experience, with copies of 3 recent testimonials to the Hospital Secretary by 17th December, 1958.

MIDDLESEX HOSPITAL, W.1. Applications invited for post of REGISTRAR in the Department of Radiotherapy.

Forms of application, obtainable from the Deputy Superintendent, should be returned, naming 2 referees, by 29th November.

MIDDLESEX HOSPITAL, W.1. Applications invited for post of SURGICAL REGISTRAR.

Rules and application forms, obtainable from the Deputy Superintendent, should be returned, naming 2 referees, by 29th November.

NELSON HOSPITAL, Kingston-road, Merton, S.W.20. (123 Beds.) HOUSE SURGEON (resident, approved for pre-registration service). Post vacant end November.

Applications, stating age, qualifications, &c., and the names and addresses of 2 referees, to the Secretary at above address.

NORTH MIDDLESEX HOSPITAL, London, N.18. Locum REGISTRAR in Surgery required for 2 weeks starting 24th November. Candidates should hold higher qualification in surgery and must have had considerable experience in emergency surgery. Further details on request. Non-resident post, but Registrar is required to sleep in hospital on full duty nights.

Applications, with full particulars and copies of testimonials or names of 2 referees, to Secretary of Hospital.

PLAISTOW HOSPITAL, Samson-street, London, E.13. (211 Beds.) Applications are invited for the appointment of RESIDENT HOUSE OFFICER (post-registration or pre-registration second post) for 6 months commencing mid-November, in the Chest Unit and Infectious Diseases Unit. Some experience in diseases of the chest desirable. The position offers good opportunities for experience in general medicine.

Applications, with copies recent testimonials, to Hospital Secretary by 5th November.

PRINCE OF WALES'S GENERAL HOSPITAL. Applications are invited for the appointment of RESIDENT PÆDIATRIC HOUSE PHYSICIAN (third post) to the above Hospital for a period of 6 months, vacant on 24th November, 1958 (post recognised for D.C.H.).

Application form from Secretary, Tottenham Group Hospital Management Committee, The Green, N.15, to be returned by 10th November, 1958.

ROYAL FREE HOSPITAL GROUP. Applications are invited from registered Women medical practitioners for 2 resident posts of REGISTRAR in Gynæcology and Obstetrics :—

1. To work at Elizabeth Garrett Anderson Hospital from 1st December, 1958.
2. To work at Elizabeth Garrett Anderson and Hampstead General Hospitals, from 1st January, 1959.

Appointments for 1 year in the first instance.

Application forms may be obtained from the Secretary to the Board of Governors, The Royal Free Hospital, Gray's Inn-road, W.C.1, to whom they should be returned not later than 7th November, 1958.

ROYAL FREE HOSPITAL GROUP. Applications are invited for the post of non-resident SENIOR MEDICAL REGISTRAR. Duties to commence on 1st January, 1959. Appointment for 1 year in the first instance. Candidates should be registered medical practitioners and members of the Royal College of Physicians.

Formal application, giving details of experience, &c., together with the names of 3 referees, should be sent to the Secretary to the Board of Governors, The Royal Free Hospital, Gray's Inn-road, W.C.1, by 14th November, 1958.

ROYAL FREE HOSPITAL GROUP. Applications are invited for 2 posts of MEDICAL REGISTRAR. Candidates should be Members of the Royal College of Physicians. The appointments are for 1 year in the first instance, duties to commence 1st January, 1959.

Application forms may be obtained from the Secretary to the Board of Governors, The Royal Free Hospital, Gray's Inn-road, W.C.1, to whom they should be returned not later than 14th November, 1958.

ROYAL FREE HOSPITAL. Applications are invited from registered medical practitioners for the post of SENIOR CASUALTY OFFICER. The appointment is full time, resident, for 6 months, duties to commence on 1st January, 1959. Salary and conditions of service in accordance with those laid down by the Ministry of Health for Senior House Officers.

Application forms may be obtained from the Secretary to the Board of Governors, The Royal Free Hospital, Gray's Inn-road, W.C.1, to whom they should be returned as soon as possible.

ROYAL FREE HOSPITAL, W.C.1, and WHITTINGTON HOSPITAL, N.19. Applications are invited for the post of REGISTRAR to the Departments of Physical Medicine at the Royal Free and Whittington Hospitals. Duties to commence at the Whittington Hospital. Appointment is full-time, non-resident, and for 1 year in the first instance, starting 1st January, 1959.

Applications, with the names of 2 referees, should be made to the Secretary to the Board of Governors, Royal Free Hospital, Gray's Inn-road, W.C.1, by 30th November, 1958.

ROYAL FREE HOSPITAL and HEATHERWOOD ORTHOPÆDIC HOSPITAL, ASCOT. (REGIONAL ORTHOPÆDIC CENTRE.) Applications are invited from registered medical practitioners for the post of SENIOR ORTHOPÆDIC REGISTRAR (non-resident) to work for a maximum period of 2 years at each hospital. The successful candidate would be required to participate in the Windsor Accident Service whilst at Heatherwood.

Formal applications, giving 3 names for reference, should be made to the Secretary to the Board of Governors, The Royal Free Hospital, Gray's Inn-road, W.C.1, by 12th November, 1958.

ROYAL FREE HOSPITAL and HEATHERWOOD ORTHOPÆDIC HOSPITAL. (REGIONAL ORTHOPÆDIC CENTRE.) Applications are invited from registered medical practitioners for the post of ORTHOPÆDIC REGISTRAR (non-resident) to work for a maximum period of 1 year at each Hospital, duties to commence on 1st January, 1959.

Application forms may be obtained from the Secretary to the Board of Governors, The Royal Free Hospital, Gray's Inn-road, W.C.1, to whom they should be returned by 12th November, 1958.

ROYAL NORTHERN HOSPITAL, Holloway, N.7. Applications are invited for the post of CASUALTY OFFICER (Senior House Officer grade) with duties in the E.N.T. Department, vacant mid-November. Recognised for F.R.C.S.

Applications, with copies of recent testimonials, to be sent to the Hospital Secretary by 11th November, 1958.

ROYAL NORTHERN HOSPITAL, Holloway, N.7. Applications are invited for the post of HOUSE PHYSICIAN (post- or pre-registration), vacant 16th December, 1958.

Applications, with copies of recent testimonials, to be sent to the Hospital Secretary by 11th November.

THORPE COOMBE MATERNITY HOSPITAL, Walthamstow, E.17. (58 Beds.) Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER. Experience in obstetrics is essential. Salary £819 10s. p.a. less £150 p.a. for board-residence.

Applications, with full details and copies of 2 recent testimonials, should be sent to Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

SOUTH LONDON HOSPITAL FOR WOMEN AND CHILDREN, Clapham Common, London, S.W.4. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited from registered Women medical practitioners for the post of Full-time SURGICAL REGISTRAR (recognised for the F.R.C.S.). Successful candidate must be prepared to live within 20 minutes of the Hospital. Vacant now. The appointment is normally for 2 years but subject to review at the end of the first year. Candidates are invited to visit the Hospital by local arrangement.

Forms of application from the Secretary, Lambeth Group Hospital Management Committee, Renfrew-road, S.E.11, to whom completed applications should be returned not later than 15th November, 1958.

ST. JAMES' HOSPITAL, Balham, London, S.W.12. South WEST METROPOLITAN REGIONAL HOSPITAL BOARD. E.N.T. REGISTRAR (resident) required. Post now vacant.

Application forms, obtainable from Group Secretary, Wandsworth Hospital Group, at above address, to be completed and returned by 15th November.

ST. JAMES' HOSPITAL, Balham, S.W.12. Wandsworth HOSPITAL GROUP. SENIOR HOUSE OFFICER (orthopædic and traumatic surgery) required 19th November. Post recognised for F.R.C.S.

Applications, stating age, qualifications and experience, with copies of 2 recent testimonials, to Group Secretary at above address by 8th November.

ST. MARY'S HOSPITAL, W.2. Registrar in General Medicine (whole-time, non-resident) for first period of 12 months from 1st January, 1959, to undertake work in Casualty and Outpatient Departments, together with certain inpatient duties.

Applications, giving full details, with names and addresses of 3 referees, should reach the House Governor not later than 10th November, 1958.

ST. MARY'S HOSPITAL, W.2. Resident House Physician to the Neurological, Dermatological, and Venereological Departments, for 6 months from 1st December, 1958. Second pre-registration or post-registration candidates are eligible to apply.

Applications, giving full details, and names and addresses of 3 referees, should reach the House Governor not later than 4th November, 1958.

ST. MARY'S HOSPITAL, W.2. Resident Anæsthetist (Senior House Officer) for a first period of 6 months from 1st January, 1959.

Applications, giving full details, with names and addresses of 3 referees, should reach the House Governor not later than 11th November, 1958.

ST. MATTHEW'S HOSPITAL, Shepherdess-walk, London, N.1. Applications are invited from registered medical practitioners for the post of SENIOR HOUSE OFFICER at this Geriatric Hospital of 320 Beds.

Apply to the Hospital Secretary, stating experience, with copies of recent testimonials, by 15th November, 1958.

ST. THOMAS'S HOSPITAL, London, S.E.1. Surgical REGISTRAR (2 vacancies). For a period of 1 year in the first instance. There are 4 Surgical Registrar posts at St. Thomas's and in the Group which are interchangeable, 2 of them being resident and 2 non-resident.

Applications, naming 2 referees, to Clerk of the Governors by 8th November, 1958.

ST. THOMAS'S HOSPITAL, London, S.E.1. Resident ASSISTANT PHYSICIAN (Senior Registrar grade). For a period of 1 year in the first instance from 15th February, 1959. Renewable for a second year.

Applications, naming 2 referees, to Clerk of the Governors by 15th November, 1958.

WANSTEAD HOSPITAL, Hermon Hill, E.11. (191 Beds.) Applications are invited for the post of OBSTETRIC AND GYNÆCOLOGICAL HOUSE SURGEON, vacant 17th November, 1958. The appointment is recognised for D.Obst.R.C.O.G.

Applications, with full details and copies of 2 recent testimonials, should be sent immediately to Secretary, Hospital Management Committee, Forest Group, Langthorne-road, E.11.

WANSTEAD HOSPITAL, Hermon Hill, London, E.11. (191 Beds.) HOUSE PHYSICIAN required.

Applications, with full details and copies of 2 recent testimonials, should be sent immediately to Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY, 91, Dean-street, W.1. Applications are invited for the post of SENIOR HOUSE PHYSICIAN (organic neurology).

Applications, stating age, qualifications and experience, together with the names and addresses of 2 referees, to be forwarded to the Hospital Secretary by 8th November, 1958.

WHIPPS CROSS HOSPITAL, Leytonstone, E.11. Leytonstone (NO. 10) HOSPITAL GROUP. Applications are invited for the post of PÆDIATRIC HOUSE OFFICER (pre- or post-registration) at above Hospital. This post, which is recognised for the D.C.H., becomes vacant 1st December, 1958.

Application forms are obtainable from the Hospital Secretary, to be returned by 11th November, 1958.

WIMBLEDON HOSPITAL, Thurston-road, Copse Hill, S.W.20. (82 Beds.) RESIDENT HOUSE SURGEON (not pre-registration). Post vacant 25th November. Salary £577 10s. Post affords good opportunity for postgraduate training and offers excellent experience in surgery.

Applications, giving age, qualifications, &c., and names and addresses of 2 referees, to the Secretary at above address.

ABERGAVENNY. PEN-Y-VAL AND MAINDIFF COURT HOSPITALS. VALE OF USK HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER at above Hospital. The appointment offers widely varied experience in all branches of psychiatry. Maindiff Court is a modern early-treatment psychiatric unit with electroencephalographic and ancillary departments. Duties include attendance at outpatient clinics, including child guidance. Opportunities provided for attendance at courses for D.P.M. Salary according to national scales. House or residential accommodation available.

Applications, together with the names of 2 referees, to be forwarded immediately to the Medical Superintendent, Pen-y-val Hospital, Abergavenny.

ABERYSTWYTH, CARDIGANSHIRE. GENERAL HOSPITAL. MID-WALES HOSPITAL MANAGEMENT COMMITTEE. HOUSE OFFICER (surgical) required (resident). Post recognised for F.R.C.S. examination. Vacancy immediate.

Applications, stating age, experience, &c., to the Group Secretary, Mid-Wales Hospital Management Committee, 31, North-parade, Aberystwyth, Cardiganshire.

ASHFORD HOSPITAL, Ashford, Middlesex. (560 Beds.) STAINES GROUP HOSPITAL MANAGEMENT COMMITTEE. Required, RESIDENT HOUSE SURGEON for general surgical duties. 6 months' appointment. Preference given to pre-registration candidates. Post vacant 27th November, 1958.

Applications, stating age, qualifications and experience, with copies of up to 3 recent testimonials, to Medical Director of Hospital immediately.

ASHFORD HOSPITAL, Ashford, Middlesex. North West METROPOLITAN REGIONAL HOSPITAL BOARD. SURGICAL REGISTRAR for General Surgery required. Post vacant 1st December, 1958. Cottage may be available in hospital grounds for married applicant. Hospital may be visited by direct appointment with the Medical Director.

Application forms obtainable from, and returnable to, the Secretary, Ashford Hospital, London-road, Ashford, Middlesex, by 11th November, 1958.

ASHTON-UNDER-LYNE GENERAL HOSPITAL. ASHTON, HYDE AND GLOSSOP HOSPITAL MANAGEMENT COMMITTEE. JUNIOR HOSPITAL MEDICAL OFFICER (resident) required for Casualty Department at above Hospital. Appointment limited to 4 years. Minimum commencing salary £852 10s. p.a., but higher salary may be paid according to experience and qualifications. There may be some orthopædic duties to be undertaken by the holder of this post. Recognised under F.R.C.S. regulations. Vacant December.

Apply, giving age, experience, qualifications, and names of 2 referees, to Group Secretary, General Hospital, Ashton-under-Lyne.

ASHTON-UNDER-LYNE GENERAL HOSPITAL. ASHTON, HYDE AND GLOSSOP HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (pædiatrics) required at above Hospital. Neonatal experience would be especially valuable. Modern pædiatric and premature baby units. Recognised for D.C.H.

Applications, with copies of 2 references, to Group Secretary, General Hospital, Ashton-under-Lyne, Lancs.

BARNSTAPLE. NORTH DEVON INFIRMARY. (105 Beds.) HOUSE PHYSICIAN (pre-registration) required immediately.

Applications, naming 2 referees, to Group Secretary, North Devon Hospital Management Committee, 19, Alexandra-road, Barnstaple.

BEDFORD GENERAL HOSPITAL. (424 Beds.) Resident HOUSE SURGEON (gynæcology and obstetrics). Vacant mid-December. Post recognised for D.Obst.R.C.O.G. The Maternity Unit comprises 71 obstetric and 23 gynæcological beds, and the Hospital has a busy Outpatient Department.

Detailed applications, with copies of 2 recent testimonials, to Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford, by 13th November.

BEVERLEY, YORKSHIRE. WESTWOOD HOSPITAL. ASSISTANT PATHOLOGIST (Senior House Officer grade) required for Area Laboratory. Offers experience in all branches of pathology.

Detailed applications to Group Secretary.

BIRMINGHAM ACCIDENT HOSPITAL AND REHABILITATION CENTRE, Bath-row, BIRMINGHAM, 15. SENIOR HOUSE SURGEON, vacancy mid-December. Hospital is the largest traumatic unit in the country, treating 50,000 new patients a year, including 2000 burns. Ample opportunity for practical experience in all types of injury. Recognised for casualty training by Royal College of Surgeons.

Applications, naming 2 referees, to Administrator.

BIRMINGHAM ACCIDENT HOSPITAL, Bath-row, BIRMINGHAM, 15. (215 Beds and 8 House Surgeons.) HOUSE SURGEONS (resident) required from December onwards. Hospital treats over 50,000 injured patients each year, and is recognised for purpose of casualty training by R.C.S. (Eng.). 6-month appointment, part of which may be spent in 42-bedded segregated Burns Unit.

Apply, naming 2 referees, to Administrator.

BIRMINGHAM, 18. ALL SAINTS' HOSPITAL. RegisTRAR (psychiatry). All Saints' Hospital (1002 Beds) and Early Treatment Centre, Uffculme. Hospital associated with Birmingham University for teaching and research. Candidates should be actively interested in research. Resident post. Married accommodation available.

Applications to the Medical Superintendent.

BIRMINGHAM (near). MARSTON GREEN MATERNITY HOSPITAL, Berwicks-lane, MARSTON GREEN, near BIRMINGHAM. HOUSE SURGEON (obstetrics) required. Vacant 1st January, 1959. 121 obstetric and 10 gynæcological beds. Post recognised for diploma and obstetrics part of M.R.C.O.G. Premature Baby Unit. Hospital affiliated to Birmingham Medical School for training of students.

Detailed applications, with copies of 3 recent testimonials, to the Group Secretary, Dudley Road Hospital, Birmingham, 18.

BIRMINGHAM REGIONAL HOSPITAL BOARD. Wholetime SENIOR SURGICAL REGISTRAR, North Staffs Royal Infirmary. Wide experience specialty and higher qualification required. Successful candidate may subsequently be required to spend not more than 2 years in a selected hospital of the United Birmingham Hospitals in accordance with the arrangements for interchange of Senior Registrars agreed between the 2 Boards.

Application forms from Secretary, 10, Augustus-road, Birmingham, 15, to be returned by 17th November, 1958.

BIRMINGHAM REGIONAL HOSPITAL BOARD. BirmINGHAM REGIONAL BLOOD TRANSFUSION SERVICE require 1 or more Part-time MEDICAL PRACTITIONERS to undertake a total of 4 notional half-days weekly. Duties attending blood-donor sessions in the region. Remuneration £183 5s. per session p.a.

Applications (10 copies), naming 3 referees, to the Secretary, 10, Augustus-road, Birmingham, 15, by 17th November, 1958. Further information from Director, Blood Transfusion Service, 15, Ampton-road, Birmingham, 15, by appointment.

BIRMINGHAM REGIONAL HOSPITAL BOARD.

(1) Wolverhampton Group, The Royal Hospital, Wolverhampton

(*a*) REGISTRAR (orthopædics and traumatic surgery), The Royal Hospital, Wolverhampton. All types of traumatic and orthopædic conditions, also industrial work and rehabilitation, which is carried out at a special unit of 60 Beds. Married quarters available.

(*b*) REGISTRAR (surgical) required. Resident. Duties in Royal Hospital and New Cross Hospital.

(2) Birmingham (Selly Oak) Group, Oak Tree-lane, Birmingham, 29

(*a*) REGISTRAR (orthopædic), Royal Orthopædic Hospital, Birmingham. F.R.C.S. or Primary and experience in orthopædic surgery desirable. Scheme of interchange, at Registrar level, with the General Hospital, Birmingham, Casualty Department—a teaching hospital—in operation. Successful candidate may be required to spend not more than 1 year in such interchange.

(*b*) REGISTRAR (general surgery), Solihull Hospital, Lode-lane, Solihull. Resident. Single quarters only available. Higher qualification desirable.

(3) South Worcestershire Group. Worcester Royal Infirmary, Worcester

REGISTRAR (general surgery), Worcester Royal Infirmary (213 Beds) and Ronkswood Hospital, Worcester (243 Beds). Higher qualification desirable. Application made for post to be recognised for F.R.C.S.

Application forms from Group Secretaries, to be returned by 10th November, 1958.

BIRMINGHAM AND MIDLAND EYE HOSPITAL, Church-street, BIRMINGHAM, 3. (156 Beds.) HOUSE OFFICER (resident) required. Recognised for D.O. and F.R.C.S. in Ophthalmology. Wide experience available in all branches, including surgery.

Detailed applications to the Group Secretary, Dudley Road Hospital, Birmingham, 18.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for the post of SENIOR REGISTRAR in Clinical Pathology to the United Birmingham Hospitals. The appointment will be for 1 year in the first instance, and duties will be primarily at the Queen Elizabeth Hospital. Candidates should hold a higher qualification. The successful candidate may be required to spend not more than 2 years in a selected hospital of the Birmingham Regional Hospital Board in accordance with an arrangement for the interchange of Registrars agreed between the 2 Boards.

Application forms may be obtained from the Secretary to the Board, United Birmingham Hospitals, Queen Elizabeth Hospital, Birmingham, 15, and should be returned to him not later than 15th November, 1958.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. THE CHILDREN'S HOSPITAL, Ladywood-road, BIRMINGHAM, 16. HOUSE OFFICERS (surgical) required, to commence duty on 7th January, 1959, for 6 months. The posts rotate during the period, giving good experience of general and special surgery. Recognised for pre-registration students, but registered practitioners may apply.

Forms of application available from the House Governor, and should be returned to him by 2nd November, 1958.

G. A. PHALP, Secretary to the Board of Governors.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. THE CHILDREN'S HOSPITAL, Ladywood-road, BIRMINGHAM, 16. Applications are invited for the post of ASSISTANT RESIDENT MEDICAL OFFICER, vacant 7th January, 1959, for 6 months to take charge of Infants Block (66 Cots), followed by 6 months as Resident Medical Officer in charge of the main wards. Valuable opportunity for further study of disease of infancy, some previous experience of which is desirable. M.R.C.P. preferred. Both posts Senior House Officer grade.

Forms of application available from the House Governor and should be returned to him by 22nd November, 1958.

G. A. PHALP, Secretary to the Board of Governors.

BISHOP AUCKLAND. THE GENERAL HOSPITAL. HOUSE OFFICER (obstetrics and gynæcology). Applications invited from registered or pre-registration practitioners. Vacant 1st January, 1959. Recognised for D.Obst.R.C.O.G. Departmental beds 69.

Apply, naming 2 referees, to Group Secretary, South West Durham Hospital Management Committee, at above address.

BLACKBURN AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. JUNIOR HOSPITAL MEDICAL OFFICER required immediately for established Geriatric Department under control of Consultant Geriatrician. There are 360 geriatric beds at Queen's Park Hospital, Blackburn, Springfield Hospital, Blackburn, and Clitheroe Hospital, Clitheroe. Accommodation for married man may be available if required.

Applications, with names and addresses of 2 referees, to Group Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

BLACKPOOL. VICTORIA HOSPITAL. Blackpool and FYLDE HOSPITAL MANAGEMENT COMMITTEE. MANCHESTER REGIONAL HOSPITAL BOARD. Applications are invited for the post of REGISTRAR in the Department of Diagnostic Radiology at the above Hospital which is recognised for the D.M.R.D. Part II. The post offers wide experience in all aspects of the work of a busy hospital group, including that of thoracic surgery, the Hospital being the Centre for this specialty for the northern part of the Manchester Region.

The Department may be visited by arrangement with the Group Secretary, Victoria Hospital, Blackpool, to whom applications, stating age, qualifications, experience, and the names and addresses of 2 referees, should be sent.

BLACKPOOL VICTORIA HOSPITAL. (354 Beds.) HOUSE SURGEON. Resident pre-registration post available from 12th November, 1958, in the Department of Surgery at this well-equipped Hospital with excellent facilities for gaining experience. Recognised for F.R.C.S.

Applications, stating age, experience, and the names and addresses of 2 referees, should be sent to the Hospital Secretary.

BOLTON DISTRICT GENERAL HOSPITAL (607 Beds, including 107 for obstetrics and 30 for gynæcology). RESIDENT HOUSE OFFICER for the Department of Obstetrics and Gynæcology. Vacant early December, tenable for 6 months and recognised under the pre-registration service scheme. Also recognised for M.R.C.O.G. and D.Obst.R.C.O.G.

Applications, stating age, nationality, qualifications, experience and names of 2 referees, should be sent to Group Secretary, Bolton and District Hospital Management Committee, The Royal Infirmary, Bolton, not later than 7th November, 1958.

BRADFORD A AND B HOSPITAL MANAGEMENT COMMITTEES. JUNIOR HOUSE OFFICER required for Geriatric Admission Unit. Post vacant now. Major portion of duties carried out at St. Luke's Hospital, Bradford.

Applications, stating age, nationality, qualifications and experience, with copy testimonials, to the Secretary, Royal Infirmary, Bradford, Yorks.

BRADFORD, YORKSHIRE. ST. LUKE'S HOSPITAL. (724 Beds.). HOUSE SURGEON (general surgery) required for 1st November, 1958. Post recognised for F.R.C.S. and pre-registration purposes.

Applications, stating age, qualifications, nationality, &c., to the Secretary, Royal Infirmary, Bradford.

BRADFORD ROYAL INFIRMARY. (507 Beds.) House SURGEON (orthopædics (casualty) required 1st November, 1958. Post recognised for F.R.C.S. and pre-registration purposes.

Applications, stating age, qualifications, nationality, &c., to the Secretary.

BRADFORD ROYAL INFIRMARY. (507 Beds.) House SURGEON (general surgery) required 1st November, 1958. Post recognised for F.R.C.S. and pre-registration purposes.

Applications, stating age, qualifications, nationality, &c., to the Secretary.

BRADFORD ROYAL INFIRMARY. (507 Beds.) House SURGEON (general surgery,urology) required 1st November, 1958. Post recognised for F.R.C.S. and pre-registration purposes.

Applications, stating age, qualifications, nationality, &c., to the Secretary.

BOURNEMOUTH. ROYAL VICTORIA HOSPITAL, Shelley-road. BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of HOUSE SURGEON (general surgery). The appointment, which becomes vacant on 1st December, 1958, is recognised for the F.R.C.S. examination and for pre-registration purposes.

Applications to the Hospital Secretary.

BOURNEMOUTH. ROYAL VICTORIA HOSPITAL, Shelley-road. BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of 3 SENIOR HOUSE OFFICERS (orthopædics and casualty). These appointments, which become vacant on 15th December and 21st December, 1958, and 18th January, 1959, are recognised for the F.R.C.S. examination. The Unit now consists of 3 Senior House Officers and a Registrar.

Applications to the Hospital Secretary.

BRIGHTON GENERAL HOSPITAL. Applications are invited for the pre-registration appointment of HOUSE SURGEON (orthopædics).

Applications, stating age, qualifications, and the names of 2 referees, should be sent to the Physician-Superintendent, Brighton General Hospital, Elm-grove, Brighton.

BRIGHTON. NEW SUSSEX HOSPITAL FOR WOMEN and SUSSEX MATERNITY HOSPITAL. BRIGHTON AND LEWES HOSPITAL MANAGEMENT COMMITTEES. GYNÆCOLOGICAL AND OBSTETRIC HOUSE SURGEON (Female) required. Gynæcological Department (24 Beds) at New Sussex Hospital and relief obstetrical work at Sussex Maternity Hospital (62 Beds). Post recognised for M.R.C.O.G. (gynæcology only).

Applications, giving age, experience, and 2 references, to be sent to the Administrative Officer, New Sussex Hospital, Windlesham-road, Brighton, as soon as possible.

BRIGHTON. ROYAL SUSSEX COUNTY HOSPITAL. (314 Beds.)

HOUSE SURGEON required mid-November.

2 CASUALTY HOUSE SURGEONS required beginning and end December. Full and varied experience in busy Casualty Department (staff of 3), and, also, duties in Orthopædic and Traumatic Unit, including charge of beds.

All posts recognised for pre-registration and F.R.C.S.

Applications, stating age, qualifications, experience, and naming 2 referees, to the Administrative Officer, Royal Sussex County Hospital, Brighton, 7.

BRIGHTON. ROYAL SUSSEX COUNTY HOSPITAL. SENIOR CASUALTY OFFICER (Junior Hospital Medical Officer grade) required for busy Casualty Department (2 junior medical staff). Vacant early November. Recognised for F.R.C.S.

Applications, stating age, qualifications and experience, together with the names of 2 referees, to the Administrative Officer.

BROMSGROVE GENERAL HOSPITAL, Worcestershire. (411 Beds.) HOUSE OFFICER in Obstetrics and Gynæcology required. 38 maternity, 18 gynæcological beds. Post vacant January, 1959. Recognised for D.Obst.R.C.O.G. and M.R.C.O.G.

Applications, with the names of 3 referees, to the Hospital Secretary.

BURTON-ON-TRENT. THE GENERAL HOSPITAL. HOUSE OFFICER (orthopædics) (pre-registration post) required at the above Hospital. Recognised for F.R.C.S.

Applications to Group Secretary as soon as possible.

BURY AND ROSSENDALE HOSPITAL MANAGEMENT COMMITTEE. FAIRFIELD GENERAL HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER in Obstetrics and Gynæcology. Post recognised for D.Obst.R.C.O.G.

Apply, stating full details, and names of 2 referees, to Group Secretary, Bury General Hospital, Bury, Lancs.

CANTERBURY. KENT AND CANTERBURY HOSPITAL. (277 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (pathology) (non-resident), which is now vacant. The post is for 1 year. Salary £819 10s. p.a., with National Health Service conditions. Experience in pathology not essential, but candidates must have had previous clinical experience.

Applications, stating age, qualifications, together with copies of 2 recent testimonials, to be addressed to the Hospital Secretary at the above Hospital.

CANTERBURY. KENT AND CANTERBURY HOSPITAL. (277 Beds.) The post of GENERAL SURGICAL AND UROLOGICAL HOUSE SURGEON (pre-registration or third post), which is recognised for the F.R.C.S., will become vacant mid-November. National Health Service salary and conditions.

Applications, together with copies of 2 recent testimonials, to be addressed to the Hospital Secretary at the above Hospital.

CHELMSFORD. ST. JOHN'S HOSPITAL. (65 surgical beds.) Applications are invited for the appointment of RESIDENT SURGICAL OFFICER (Senior House Officer grade). The post, which becomes vacant on 6th December, 1958, is recognised for the F.R.C.S., and the successful candidate will gain excellent experience in general surgery, with good opportunity for preparation for higher qualifications. A House Surgeon is in residence.

Applications, stating age, nationality, qualifications and experience, with dates, together with recent testimonials, to be received not later than 17th November, 1958, by the Group Secretary, Chelmsford Group Hospital Management Committee, Chelmsford and Essex Hospital, London-road, Chelmsford.

CHELMSFORD AND ESSEX HOSPITAL. (161 Beds.) Applications are invited for the post of RESIDENT HOUSE SURGEON. Pre-registration post. The post will become vacant at the end of November, and offers good surgical experience. Recognised for the F.R.C.S.

Applications, together with 2 recent testimonials, to the Secretary, Chelmsford Hospital Management Committee, London-road, Chelmsford.

CHELMSFORD AND ESSEX HOSPITAL. (161 Beds.) Applications are invited for the post of RESIDENT HOUSE PHYSICIAN, pre-registration post, to work in the general medical wards of the Hospital. Duties will commence on 13th December.

Applications, together with 2 recent testimonials, to the Secretary, Chelmsford Hospital Management Committee, London-road, Chelmsford.

CHEDDLETON, near LEEK, STAFFORDSHIRE. ST. EDWARD'S HOSPITAL. JUNIOR HOSPITAL MEDICAL OFFICER. Previous mental hospital experience not essential. This Hospital offers opportunities for gaining experience in all branches of psychiatry. Terms and conditions of service will be as approved for hospital medical staff employed in the National Health Service. Salary £852–£55–£1182 p.a. Single furnished quarters, or unfurnished house on Hospital estate available for a married man.

Applications as soon as possible to the Medical Superintendent.

CHERTSEY, SURREY. ST. PETER'S HOSPITAL (late Botley's Park War Hospital). CASUALTY OFFICER (Senior House Officer) required from 14th November, 1958. Resident or non-resident. The appointment is mainly that of Outpatient Sorting Officer and gives time and opportunity for reading for a higher qualification. Recognised for F.R.C.S. Salary in accordance with terms and conditions of National Health Service. Applications for a 6-month appointment would be considered.

Applications, together with names and addresses of referees, to Physician-Superintendent, St. Peter's Hospital, as soon as possible.

CHESTERFIELD HOSPITAL MANAGEMENT COMMITTEE. JUNIOR HOSPITAL MEDICAL OFFICER required at Whittington Hall, Chesterfield (356 Beds for female mentally deficient patients), and Scarsdale Hospital, Chesterfield, where there are 125 Beds for mental patients. Previous experience advantageous but not essential. Post offers ample opportunities for study. Small flat available within the Group if required.

Please apply, with names of 2 referees, to the Group Secretary at the Chesterfield Royal Hospital.

COLCHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications invited for :—

Essex County Hospital, Colchester, Essex (181 Beds)

Post of SENIOR HOUSE OFFICER to Casualty and Radiotherapy Departments. Tenable for 6 months or 1 year. Recognised for F.R.C.S.

Post of SENIOR HOUSE OFFICER to E.N.T. and Pædiatric Departments. Tenable for 6 months or 1 year. Recognised for D.L.O. The Pædiatric Department consists of a new unit of 24 Beds.

Clacton and District Hospital, Clacton-on-Sea (58 Beds)

Post of SENIOR HOUSE OFFICER. Duties include medical, surgical, and casualty work. Post tenable for 6 months or 1 year.

Applications, with copies of 3 testimonials, to Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

COVENTRY AND WARWICKSHIRE HOSPITAL. (354 Beds.) CASUALTY AND ACCIDENT OFFICER (Junior Hospital Medical Officer status). Recognised F.R.C.S. Resident. This is an additional appointment to a full-time staff of Senior Hospital Medical Officer and Junior Hospital Medical Officer.

Applications to Hospital Secretary, Coventry and Warwickshire Hospital, Stoney Stanton-road, Coventry.

DUNFERMLINE AND WEST FIFE HOSPITAL. (General surgical—138 Beds.) WEST FIFE HOSPITALS BOARD OF MANAGEMENT. JUNIOR HOSPITAL MEDICAL OFFICER required for the new Casualty Department. Resident; first-class accommodation in new Doctors' residence, with possibility of providing married quarters. National Health Service Whitley Council salary and conditions of service.

Apply immediately, giving full particulars of age, qualifications and experience, and names of 3 referees, to the Consultant Surgeon, Dunfermline and West Fife Hospital, Reid-street, Dunfermline.

DERBY. CITY HOSPITAL. Derby Area No. 1 Hospital MANAGEMENT COMMITTEE. Applications are invited for the post of HOUSE PHYSICIAN (Senior House Officer—medicine) for duties in General Medicine. Post vacant 1st November.

Applications, stating full details, together with copies of 2 recent testimonials, should be sent to the Medical Superintendent, City Hospital, Derby, as soon as possible.

DERBY CITY HOSPITAL. (260 Beds.) (Recognised for training for F.R.C.S.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT or NON-RESIDENT SURGICAL REGISTRAR required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 10th November, 1958, giving age, nationality, qualifications, present and previous appointments (with dates), naming 3 referees.

DERBY. DERBYSHIRE ROYAL INFIRMARY (416 Beds), DERBY CITY HOSPITAL (260 Beds). (Post recognised for training for D.A. and F.F.A. R.C.S.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT REGISTRAR (anæsthetics) required immediately for the above Hospitals. Duties also at other hospitals in the Group. This post offers special experience in neuro and orthopædic surgery and obstetrics. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 10th November, 1958, giving age, nationality, qualifications, present and previous appointments, with dates, naming 3 referees.

DERBY. DERBYSHIRE ROYAL INFIRMARY. (416 Beds.) SENIOR HOUSE OFFICER (general surgery), resident. Vacant 2nd December. Recognised F.R.C.S.

Apply, giving full details and 2 names for reference, to Secretary.

DONCASTER ROYAL INFIRMARY. (330 Beds.) Applications are invited for the post of RESIDENT ANÆSTHETIST in the grade of Senior House Officer. Post recognised under the regulations for the F.F.A. R.C.S. and D.A.

Applications, with particulars of experience and copies of 2 recent testimonials, to the Group Secretary, Doncaster Hospital Management Committee, at Doncaster Royal Infirmary.

DORCHESTER. DORSET COUNTY HOSPITAL. House SURGEON (Male or Female) required for resident, pre-registration post now vacant. Recognised for F.R.C.S. examination and tenable for 6 months.

Applications, stating age, qualifications, together with copy testimonials, to Group Secretary, West Dorset Hospital Management Committee, Damers-road, Dorchester, Dorset, immediately.

EAST ANGLIAN REGIONAL HOSPITAL BOARD. MEDICAL REGISTRAR, West Suffolk General Hospital, Bury St. Edmunds (262 Beds). Appointment for 1 year, renewable for second year.

Applications, stating age, experience, and the names of 3 referees, to Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, by 17th November, 1958. Candidates invited to visit the Hospital by direct arrangement with Hospital Management Committee Secretary at the Hospital.

EBBW VALE HOSPITAL. (General beds 71, maternity 15.) Applications are invited for the appointment of RESIDENT SURGICAL OFFICER (Junior Hospital Medical Officer grade). The Hospital is an active Surgical Unit, and the Medical staff consists of a Resident Consultant General Surgeon and visiting Orthopædic, Gynæcological and Ophthalmic Surgeons. Furnished flat available. The tenure of the appointment shall be for a period not exceeding 4 years.

Apply, giving full details and references, to Group Secretary, North Monmouthshire Hospital Management Committee, Nevill Hall Hospital, Abergavenny, Mon.

EDGWARE GENERAL HOSPITAL, Edgware, Middlesex. (647 Beds.) 2 RESIDENT HOUSE PHYSICIANS for above Hospital. Posts vacant 26th and 29th November, 1958. 6 months' appointments. Recognised for pre-registration purposes.

Applications, stating age, qualifications, experience, and enclosing copies of up to 3 recent testimonials, to Medical Administrator of Hospital by 8th November, 1958.

EDGWARE GENERAL HOSPITAL, Edgware, Middlesex. (704 Beds.) SENIOR HOUSE SURGEON required for E.N.T. Department of above Hospital.

Applications, stating age, qualifications, experience, and enclosing names and addresses of 2 referees, to Group Secretary, Edgware General Hospital, by 8th November, 1958.

EDGWARE GENERAL HOSPITAL, Edgware, Middlesex. (647 Beds.) RESIDENT HOUSE PHYSICIAN required for above Hospital. 6 months' appointment.

Applications, stating age, qualifications and experience, and enclosing copies of up to 3 recent testimonials, to Medical Administrator of Hospital by 15th November, 1958.

ENFIELD, MIDDLESEX. CHASE FARM HOSPITAL. RESIDENT HOUSE SURGEON. Pre-registration post. Vacant 12th November, 1958. Duties with General Surgical Unit. Post recognised by the Royal College of Surgeons. 6-month appointment.

Applications, with the names and addresses of 2 referees, to the Group Secretary, Enfield Group Hospital Management Committee, Chase Farm Hospital.

EPSOM DISTRICT HOSPITAL, Dorking-road, Epsom, SURREY. RESIDENT HOUSE SURGEON. Required 11th December for general surgery. Pre-registration post recognised for F.R.C.S.

Applications, stating age, qualifications and experience, with copies of 2 recent testimonials, should be sent, as soon as possible, to Group Secretary, at above address.

GRAVESEND AND NORTH KENT HOSPITAL, Gravesend. MEDWAY AND GRAVESEND HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON required. Post, which is vacant mid-November, is recognised for the F.R.C.S. and approved for pre-registration purposes. Successful applicant will be attached to 2 Consultant Surgeons with opportunity for extensive surgery and vascular work. Salary £467 10s.–£577 10s. p.a., according to experience.

Applications to Hospital Secretary, stating age, experience, qualifications and nationality.

GRAVESEND AND NORTH KENT HOSPITAL, Gravesend. MEDWAY AND GRAVESEND HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the resident post of HOUSE PHYSICIAN which becomes vacant towards end of November. Approved for pre-registration purposes. Salary £467 10s.–£577 10s. according to experience.

Applications to Hospital Secretary stating age, experience, qualifications and nationality.

GRIMSBY. SCARTHO ROAD HOSPITAL. Grimsby HOSPITAL MANAGEMENT COMMITTEE. RESIDENT HOUSE OFFICER (surgical) required. Pre-registration or Senior House Officer grade for duties in acute surgical unit of 43 Beds, modern theatre and Outpatient Department. Offers excellent experience of all types of general surgery. Good married quarters available. Post vacant mid-December, 1958.

Applications, with names of 2 referees, to Hospital Secretary.

HEMEL HEMPSTEAD. WEST HERTS HOSPITAL. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. ANÆSTHETIC REGISTRAR required at above Hospital. Post recognised for F.F.A. R.C.S. Post vacant immediately.

Application form obtainable from and returnable to Secretary, West Herts Group Hospital Management Committee, 9, Rickmansworth-road, Watford, Herts, by not later than 18th November, 1958.

HEMEL HEMPSTEAD. ST. PAUL'S AND WEST HERTS HOSPITALS. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR in Clinical Pathology required at above Hospitals. Post now vacant. Hospitals may be visited by direct appointment.

Application form obtainable from and returnable to Secretary, West Herts Group Hospital Management Committee, 9, Rickmansworth-road, Watford, Hertfordshire, by not later than 18th November.

HALIFAX. ST. JOHN'S HOSPITAL. (382 Beds.) Senior HOUSE OFFICER for Geriatrics and long-stay medical cases required. Post vacant. Consultant Geriatrician in charge. X-ray, pathological laboratory, occupational therapy and physiotherapy services provided; opportunity for study.

Applications to Group Secretary, Royal Halifax Infirmary, Halifax.

HAREFIELD HOSPITAL, Harefield, Middlesex. Applications are invited for the post of RESIDENT ANÆSTHETIST (Senior House Officer) for duties on the Thoracic Surgical Unit.

Applications, together with copies of 2 testimonials, to be sent to the Medical Director, Harefield Hospital, Harefield, Middlesex, by 17th November, 1958.

HEREFORD. COUNTY HOSPITAL. (341 Beds.) House OFFICER (obstetrics and gynæcology) required immediately, pre-registration post.

Applications, with copies of 2 testimonials, to be sent to the Medical Superintendent, County Hospital, Hereford.

HEREFORD COUNTY HOSPITAL. (341 Beds.) House OFFICER (surgery) required immediately, pre-registration post. Hospital recognised for F.R.C.S.

Applications, with copies of 2 recent testimonials, to Medical Superintendent, County Hospital.

HEREFORD. GENERAL HOSPITAL. (154 Beds.) House OFFICERS (general surgery) required, pre-registration posts. 1 vacancy immediately, 1 post vacant 15th December. Hospital recognised by R.C.S. Duties include care of general surgical beds, and in addition for 3 months of orthopædic beds and for 3 months of E.N.T. beds.

Applications, with copies of 2 testimonials, to be sent to the Group Secretary, Victoria House, Eign-street, Hereford.

HEREFORD GENERAL HOSPITAL. (154 Beds.) Locum SENIOR HOUSE OFFICER (surgery) required immediately.

Applications, with copies of 2 testimonials, to be sent to the Administrative Officer, General Hospital, Hereford.

HOUNSLOW HOSPITAL, Staines-road, Hounslow, MIDDLESEX. (General acute—81 Beds.) Applications are invited for the appointment of RESIDENT HOUSE SURGEON. Recognised pre-registration appointment for 6 months. Vacant 1st November, 1958.

Applications, stating qualifications and age, together with copies of 3 recent testimonials or names for reference, to the Hospital Secretary.

HUDDERSFIELD ROYAL INFIRMARY. (285 Beds.) HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. 3 HOUSE SURGEONS required to commence duty immediately. The posts are recognised as pre-registration appointments and for the F.R.C.S. Salary in accordance with national scale.

Applications, together with copies of 3 recent testimonials, to be addressed to the undersigned as soon as possible.

H. J. JOHNSON, Group Secretary,
Huddersfield Hospital Management Committee,
The Royal Infirmary, Huddersfield.

HULL. KINGSTON GENERAL HOSPITAL. (419 Beds.) HULL A GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT HOUSE SURGEON (recognised for the F.R.C.S. examination). Pre-registration post.

Applications, with 2 recent testimonials, to the Hospital Secretary.

HUNTINGDON COUNTY HOSPITAL, Huntingdonshire. Applications are invited for the post of HOUSE OFFICER (medical), now vacant. Post recognised for pre-registration purposes. The selected candidate will be required to look after medical and paediatric cases and may be called upon to give emergency anæsthetics.

Apply, with full particulars, and names of 2 referees, to Secretary, County Hospital, Huntingdon.

ILFORD. KING GEORGE HOSPITAL, Eastern-avenue, ILFORD, ESSEX. There will be the following vacancies for HOUSE SURGEONS at above Hospital:—

First or second post pre-registration. 17th November.
Second post pre-registration. 17th November.
First or second post pre-registration. 19th November.
All posts will be tenable for 6 months.

Applications, giving full particulars and accompanied by testimonials, should be sent to the undersigned within 7 days of the appearance of this advertisement.

H. F. HARRIS, Group Secretary,
Ilford and Barking Group Hospital Management Committee.

ISLEWORTH. WEST MIDDLESEX HOSPITAL. South WEST MIDDLESEX HOSPITAL MANAGEMENT COMMITTEE. HOUSE OFFICER, Traumatic and Orthopædic Surgery Unit (58 Beds). Recognised for F.R.C.S. Post vacant 4th December, 1958. Pre-registration or registered candidates.

Applications, stating age, qualifications, and experience, with copies of up to 2 testimonials, to Group Secretary, South West Middlesex Hospital Management Committee, West Middlesex Hospital, Isleworth, by 11th November, 1958.

ISLEWORTH. WEST MIDDLESEX HOSPITAL. North WEST METROPOLITAN REGIONAL HOSPITAL BOARD. SENIOR REGISTRAR in Anæsthetics (non-resident), West Middlesex Hospital and neighbouring hospitals. Regional training scheme includes facilities for gaining experience in specialised techniques at Regional Thoracic Surgical and Neurosurgical Centres. Hospital may be visited by direct appointment.

Application forms obtainable from, and returnable to, Group Secretary, South West Middlesex Hospital Management Committee, West Middlesex Hospital, Isleworth, by 11th November, 1958.

IPSWICH AND EAST SUFFOLK HOSPITAL (Anglesea-ROAD WING). (350 Beds.) Applications invited for 2 posts of HOUSE SURGEON—1 to the Senior Consultant General Surgeon and the other to 2 Consultant General Surgeons. Posts recognised for pre-registration and F.R.C.S. examinations.

Applications, with copies of recent testimonials, to Hospital Secretary.

IPSWICH. FOXHALL HOSPITAL. (Actively engaged in the investigation and treatment of all forms of chest disease, including Respiratory Physiology Department and major surgery.) SENIOR HOUSE OFFICER required early November for duties mainly on non-tuberculous and surgical wards. Married quarters available.

Further particulars from Dr. G. R. MCNAB, Physician-Superintendent, to whom applications should be made.

IPSWICH. ST. HELEN'S HOSPITAL. (129 Beds for infectious diseases, pulmonary tuberculosis, long-stay orthopædics and geriatrics. The area Chest Clinic is in the Hospital.) HOUSE PHYSICIAN required (post-registration appointment). Accommodation available for married man.

Applications to JOHN WILLIAMS, Group Secretary, Ipswich Group Hospital Management Committee, at the Ipswich and East Suffolk Hospital (Anglesea-road Wing), Ipswich.

KETTERING AND DISTRICT GENERAL HOSPITAL. CASUALTY OFFICER (Senior House Officer). Recognised for F.R.C.S. The post, vacant now, offers wide experience of all traumatic conditions including fractures and some orthopædic cases, with charge of 30 Beds.

Applications, accompanied by testimonials, to be sent to the Group Secretary, General Hospital, Kettering.

KETTERING AND DISTRICT GENERAL HOSPITAL, NORTHAMPTONSHIRE. Applications are invited for the post of HOUSE SURGEON (pre-registration) which becomes vacant on 1st December, 1958. Post recognised for F.R.C.S.

Applications, stating age, experience and qualifications, together with copies of 3 recent testimonials, to be sent to the Group Secretary at the above address.

KETTERING GENERAL HOSPITAL, Kettering. (144 Beds.) Applications are invited from registered medical practitioners for the post of SENIOR HOUSE OFFICER in Anæsthetics, vacant 4th November, 1958. Post recognised for D.A.

Applications, giving details of qualifications and experience, and enclosing copies of 3 recent testimonials, to be sent to the Group Secretary, Kettering and District Hospital Management Committee, at the above address.

KIDDERMINSTER AND DISTRICT GENERAL HOS-PITAL, WORCESTERSHIRE. Applications are invited for the pre-registration post of HOUSE SURGEON at the above Hospital.

Applications, with the names of 3 referees, to the Hospital Secretary.

KINGSTON HOSPITAL, Wolverton-avenue, Kingston-ON-THAMES. KINGSTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified medical officers for the post of SENIOR HOUSE OFFICER (casualty and orthopædic) which is now available. The post is recognised for F.R.C.S. purposes in Casualty.

Applications, stating age, qualifications and experience, together with 2 recent testimonials, should reach the Physician-Superintendent of the Hospital as soon as possible.

KINGSTON HOSPITAL, Wolverton-avenue, Kingston-ON-THAMES. KINGSTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified medical officers for the post of SENIOR HOUSE OFFICER (E.N.T.) which is available on 1st December, 1958. The post is recognised for D.L.O. purposes.

Applications, stating age, qualifications and experience, together with 2 recent testimonials, should reach the Physician-Superintendent of the Hospital as soon as possible.

LEAMINGTON SPA. WARNEFORD GENERAL HOS-PITAL. (211 Beds.) HOUSE SURGEON for Obstetric and Gynæcology Departments. New Obstetric Block of 50 Beds. Post vacant 6th December. Recognised for D.Obst.R.C.O.G.

Apply Hospital Secretary, together with copy testimonials.

LEEDS, 14. SEACROFT HOSPITAL. Senior House OFFICER in Infectious Diseases. The Infectious Diseases Section, average bed occupancy 100, is an infectious diseases undergraduate and postgraduate training unit and a regional poliomyelitis centre. The appointment is resident and for 1 year.

Applications, with full details, and names of 2 referees, to Group Secretary, Leeds Group B Hospital Management Committee, Seacroft Hospital, Leeds, 14.

LEEDS. THE UNITED LEEDS HOSPITALS. THE MATERNITY HOSPITAL AT LEEDS. SENIOR HOUSE OFFICER required for the Pædiatric Unit for a period of 1 year. Post vacant January, 1959. Successful candidate will work under the direction of the Professor of Pædiatrics and Child Health, and be responsible to him for the supervision and management of healthy and ailing babies in the Leeds Maternity Hospital. Previous experience of resident house posts in pediatrics and or obstetrics is desirable, but not essential.

Applications, stating age, qualifications, previous posts, with dates, and the names of 2 referees, should be sent to the Secretary to the Board, the General Infirmary at Leeds, by not later than 13th November, 1958.

LEEDS (near). WOODLANDS ORTHOPÆDIC HOS-PITAL, RAWDON, near LEEDS. (112 Beds.) SENIOR HOUSE OFFICER (resident) required.

Applications, stating age and experience, with copies of 2 testimonials, to the Secretary, The Royal Infirmary, Bradford, 9, Yorkshire.

LEEDS REGIONAL HOSPITAL BOARD. Short-term LOCUM TENENS appointments in the Registrar grade are constantly available at hospitals in the area of the Board, particularly in the specialties of anæsthetics, general medicine, general and orthopædic surgery, and psychiatry.

Interested practitioners, suitably experienced, should communicate with the Secretary, Joint Registrars Committee, Park-parade, Harrogate.

LEEDS REGIONAL HOSPITAL BOARD. Registrar vacancies.

General Medicine

Regional Rheumatism Centre, Harrogate (240 Beds) (9 sessions), and Rheumatism Clinic, General Infirmary, Leeds (2 sessions). Resident at the Royal Bath Hospital, Harrogate.

General Surgery

(*a*) Clayton Hospital, Wakefield (69 general surgical beds). Duties are those of Resident Surgical Officer and may include some duties in the Casualty Department. Recognised for F.R.C.S. Married quarters available.

(*b*) Huddersfield Group (100 general surgical beds). Residential accommodation available. Duties mainly at Huddersfield Royal Infirmary. Recognised for F.R.C.S. May include some duties in the Casualty Department.

(*c*) Hull A Group. Mainly at Western and Kingston General Hospitals (120 general surgical beds). Resident. Recognised for F.R.C.S.

(*d*) Hull Royal Infirmary (80 general surgical beds) and other hospitals in the Hull A Group. Resident.

Orthopædic Surgery

(*a*) Bradford A Group Orthopædic Department. Offers excellent training in all branches of Accident and Orthopædic Surgery. Resident: detached furnished house, suitable for married person—also single accommodation available.

(*b*) Harrogate General Hospital (total beds 253)—38 orthopædic beds.

Psychiatry

(*a*) Storthes Hall Hospital, Huddersfield (2750 Beds). Resident.

(*b*) Broadgate Hospital, Beverley (650 Beds). Resident. Accommodation for single person only.

(*c*) Stanley Royd Hospital, Wakefield (2000 Beds). Recognised for D.P.M. Married and single accommodation available—married accommodation outside the Hospital).

Thoracic Surgery

Regional Thoracic Centre, Pinderfields General Hospital, Wakefield (50 thoracic surgery beds). Recognised for F.R.C.S. Accommodation for a single person.

Applications, stating age, qualifications and details of present and previous appointments with dates, together with the names and addresses of 3 referees, should be forwarded to the Secretary, Joint Registrars Committee, Park Parade, Harrogate, by 12th November, 1958.

LEEDS REGIONAL HOSPITAL BOARD. Locum Senior REGISTRAR in Ophthalmology for duties in the Leeds area. The appointment will be for approximately 3–4 months in the first instance.

Applications, stating age, qualifications, details of appointments held showing dates, with the names and addresses of 3 referees, to the Secretary, Park Parade, Harrogate, by 7th November, 1958.

LEICESTER ISOLATION HOSPITAL AND CHEST UNIT. (266 Beds.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time REGISTRAR (chest and infectious diseases) required. This Hospital offers interesting work, having units for infectious diseases and all forms of chest diseases, complete thoracic surgical unit and outpatient sessions for chest diseases and cardiology. Single accommodation is available. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 10th November, 1958, giving age, nationality, qualifications, present and previous appointments (with dates), naming 3 referees.

LEICESTER. TOWERS HOSPITAL. Sheffield Regional HOSPITAL BOARD. Whole-time SENIOR REGISTRAR (psychiatry) required for duties at the above Hospital and Children's Psychiatric Clinics in Leicester and Leicestershire. Possession of a higher qualification desirable. Appointment for 1 year in first instance reviewable annually.

Application form and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 17th November, 1958.

MANCHESTER REGIONAL HOSPITAL BOARD invites applications for post of RESIDENT or NON-RESIDENT SURGICAL REGISTRAR to Macclesfield District Group hospitals, main duties Infirmary Branch Macclesfield Hospital. Hospital recognised for F.R.C.S. regulations.

Apply immediately for application form, with names and addresses of 2 referees, to Group Secretary, Willerby House, Cumberland-street, Macclesfield.

MANCHESTER REGIONAL HOSPITAL BOARD. South MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for 2 posts as REGISTRARS in Radiotherapy at the Christie Hospital and Holt Radium Institute, Manchester. Candidates must hold either the Diploma in Radiotherapy or an F.R.C.S. or M.R.C.P.

Applications, with full details, to be forwarded to the Group Secretary, Withington Hospital, Manchester, immediately.

MANCHESTER REGIONAL HOSPITAL BOARD. JUNIOR HOSPITAL MEDICAL OFFICER (orthopædics and casualty), resident or non-resident. Period of contract to be arranged. Hours 9 A.M.–6 P.M. 5½-day week. Post now vacant.

Applications, stating age, qualifications and experience, together with copies of 2 recent testimonials, to Group Secretary, Burnley and District Hospital Management Committee, Burnley General Hospital.

MANCHESTER, 20. WITHINGTON HOSPITAL. South MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (orthopædics) required at the above Hospital. This post offers excellent experience for persons who ultimately intend to specialise in orthopædic and accident work. In addition to the routine orthopædic duties of a general hospital, the unit carries out the reconstruction surgical programme of patients from the Devonshire Royal Hospital, Buxton, which has a regional catchment area.

Applications, with full details and the names of 2 referees, to be forwarded to the Group Secretary, Withington Hospital, as soon as possible.

MANCHESTER, 20. WITHINGTON HOSPITAL. South MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT CLINICAL PATHOLOGIST (Senior House Officer grade). Previous experience in pathology not essential, the post affording opportunities for gaining experience in all branches of clinical pathology.

Applications, stating age, qualifications, present post, experience, and the names of 2 referees, to be forwarded to the Group Secretary, Withington Hospital, Manchester, 20.

MANCHESTER. BOOTH HALL CHILDREN'S HOSPITAL, BLACKLEY, MANCHESTER, 9. (380 Beds. Recognised for D.C.H.) HOUSE OFFICER (surgical), pre- or post-registration. Duties mainly general surgery and neurosurgery. Post vacant.

Applications immediately, with usual particulars and copies of 2 recent testimonials, to Group Secretary.

MANCHESTER. NORTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. The following Pre-registration HOUSE OFFICER posts are now vacant :—

Ancoats Hospital. Surgery and orthopædics.

Manchester Victoria Memorial Jewish Hospital. Surgery.

Applications, with names of 2 referees, to the Group Secretary, Crumpsall Hospital, Manchester, 8, by 10th November, 1958.

MANCHESTER. NORTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. CRUMPSALL HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER in Anæsthetics. Recognised for D.A. and F.F.A. R.C.S. Vacant 15th November, 1958.

Applications, with full details and names of 2 referees, by 10th November, 1958, to Group Secretary, Crumpsall Hospital, Manchester, 8.

MANCHESTER. UNITED MANCHESTER HOSPITALS. MANCHESTER ROYAL EYE HOSPITAL. Applications are invited for the post of REGISTRAR at the above Hospital (attached to the University Department of Ophthalmology). Whole-time post (non-resident). Tenable for 12 months, subject to renewal. Previous experience in ophthalmology essential. The terms and conditions of service for hospital medical and dental staffs will apply.

Applications to be made as soon as possible on forms obtainable from the undersigned.

H. R. NORTH, General Superintendent.

MUNDESLEY HOSPITAL, Norfolk (late The Mundesley Sanatorium). Applications are invited for the newly-created post of RESIDENT MEDICAL OFFICER (Senior House Officer status). This is a pioneer post-acute hospital and rehabilitation unit of 60 Beds, serving the whole of East Anglia, and is still in the process of development. The appointment offers unique experience in a wide range of medical and surgical convalescence, and is ideal for anyone as much interested in health and its manifestations as in disease processes. Salary £819 10s. p.a., in accordance with conditions of service issued by the Ministry of Health. Furnished house available in the grounds for a married man.

Hand-written applications, stating age, qualifications, experience, sex, and the names of 2 referees, should be addressed to the Secretary, Cromer Area Hospital Management Committee, Cliff-avenue, Cromer, Norfolk.

NEWARK GENERAL HOSPITAL. Nottingham No. 1 HOSPITAL MANAGEMENT COMMITTEE. JUNIOR HOSPITAL MEDICAL OFFICER (surgical) required for above Hospital situated on Great North Road, approximately 20 miles from Nottingham. Post offers good experience. Consultant staff attending Newark Hospital are on one or more of the Nottingham Hospitals. Flat available as married quarters. Salary and conditions of service in accordance with Ministry regulations. Duties to commence immediately.

Applications, giving names of 3 referees, should be sent to Group Secretary, Nottingham No. 1 Hospital Management Committee, General Hospital, Nottingham.

NEWCASTLE REGIONAL HOSPITAL BOARD. Locum Tenens SENIOR REGISTRAR in Anæsthetics required for Ashington Group Hospitals, Northumberland. Duties commence 1st January, 1959, for 6 months. Salary £1,500 per annum.

Applications, with names of 2 referees, to Group Secretary, Ashington Group Hospitals, Ashington, Northumberland.

NEWCASTLE REGIONAL HOSPITAL BOARD. Locum Senior REGISTRAR in Ophthalmology required for Ashington Group Hospitals, Northumberland. Duties commence 1st January, 1959, for 6 months. Salary £1,500 per annum.

Applications, with names of 2 referees, to Group Secretary, Ashington Group Hospitals, Ashington, Northumberland.

NEWCASTLE REGIONAL HOSPITAL BOARD. Locum Senior REGISTRAR in Ophthalmology for duties in the Leeds area. The appointment will be for approximately 3–4 months in the first instance.

Applications, stating age, qualifications, details of appointments held showing dates, with the names and addresses of 3 referees, to the Secretary, Park Parade, Harrogate, by 7th November, 1958.

NEWCASTLE REGIONAL HOSPITAL BOARD. Locum SENIOR REGISTRAR PSYCHIATRIST, whole-time, St. George's Hospital, Morpeth. Appointment for approximately 1 year subject to usual conditions. Accommodation available.

Applications, with names and addresses of 3 referees, to Regional Psychiatrist, Newcastle Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, immediately.

NEWCASTLE REGIONAL HOSPITAL BOARD. Junior HOSPITAL MEDICAL OFFICER, whole-time, for serological and other duties within the Regional Transfusion Centre, with occasional attendance for blood collection from donors in the area covered by the Board. Experience in serology desirable but not essential. Applicants may visit the Centre, Westgate-road, Newcastle upon Tyne, 4, by contact with the Director for further details of the post.

Applications, together with the names and addresses of 2 referees, to the Senior Administrative Medical Officer, Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 14 days.

NEWCASTLE REGIONAL HOSPITAL BOARD. Locum Tenens REGISTRAR PSYCHIATRIST, whole-time, resident at St. Luke's Hospital, Middlesbrough (563 Beds). Tenure of appointment approximately 1 year. Salary £19 5s. per week, subject to usual conditions. Small flat available. Further particulars from Regional Psychiatrist.

Applications, with names and addresses of 3 referees, to Regional Psychiatrist, Newcastle Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, immediately.

NEWCASTLE UPON TYNE. WALKER GATE HOSPITAL, Benfield-road, NEWCASTLE, 6. Applications are invited for the post of SENIOR HOUSE OFFICER in the Chest Unit at the above Hospital. The officer will be required to carry out duties assigned to him under the supervision of the Senior Chest Physician. Facilities are available for attending the D.P.H. course at the University of Durham. National Health Service terms and conditions of service.

Applications, with names and addresses of 2 referees, should be sent to the Hospital Secretary.

NEWCASTLE. THE UNITED NEWCASTLE UPON TYNE HOSPITALS. Applications are invited for the resident appointment of SENIOR HOUSE OFFICER or HOUSE OFFICER in the Department of Ophthalmology at the Royal Victoria Infirmary. The appointment is recognised for pre-registration purposes. The appointment will be for 1 year and will be subject to the terms and conditions of service of hospital medical staff in the National Health Service. The salary will be at the rate of £819 10s. p.a., subject to the appropiate deductions.

Applications, giving full details and the names and addresses of 3 referees, should be sent to the undersigned within 2 weeks of the appearance of this advertisement.

A. W. SANDERSON, House Governor and Secretary.
Royal Victoria Infirmary, Newcastle upon Tyne.

NEWCASTLE. THE UNITED NEWCASTLE UPON TYNE HOSPITALS. Applications are invited for the non-resident appointment of MEDICAL REGISTRAR at the Royal Victoria Infirmary. The post will offer scope to prepare for a higher degree. The appointment is for 1 year in the first instance and will be subject to the terms and conditions of service of hospital medical staff in the National Health Service.

Applications, giving full details and the names and addresses of 3 referees, should be sent to the undersigned within 2 weeks of the appearance of this advertisement.

A. W. SANDERSON, House Governor and Secretary.
Royal Victoria Infirmary, Newcastle upon Tyne.

NEWTON ABBOT HOSPITAL. (General section, 65 Beds.) RESIDENT SENIOR HOUSE SURGEON, Male or Female, required middle November. Married quarters available.

Applications (quoting ref. F.364.40), stating qualifications, nationality, age, with copy testimonials, to be sent to Group Secretary, Torquay District Hospital Management Committee, Torbay Hospital, Torquay, S. Devon.

NEWTON ABBOT HOSPITAL. Resident Senior House SURGEON, Male or Female, required immediately, to act as Casualty Officer and House Surgeon to special departments, together with relief duties. Ability to give outpatient anaesthetics advantageous. Married quarters available.

Applications (quoting reference F.364.41), stating qualifications, nationality, age, with copy testimonials, to be sent to the Group Secretary, Torquay District Hospital Management Committee, Torbay Hospital, Torquay, South Devon.

NORWICH, LOWESTOFT AND GREAT YARMOUTH HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR HOUSE OFFICER in Anaesthetics for duties in the first instance at the Norfolk and Norwich and Allied Hospitals in the Norwich Sub-group. Subsequently the holder of the appointment will be required to work at the Great Yarmouth and Lowestoft Hospitals. The combined appointment will be for at least 1 year. Salary £819 10s. p.a. If resident, deduction of £150 p.a. Post recognised for D.A. Membership of a medical defence society is a condition of appointment.

Applications, stating age, qualifications, and experience, with 2 names for reference, to the Group Secretary, Hospital Management Committee, St. Stephen's-road, Norwich, by 10th November, 1958.

NOTTINGHAM GENERAL HOSPITAL. Pre-registration HOUSE SURGEON required. Duties to commence immediately.

Applications, stating age, qualifications, and experience, together with copies of testimonials, to be sent to Group Secretary.

NUNEATON. MANOR HOSPITAL. House Surgeon in Orthopædics and General Surgery (pre-registration). Recognised F.R.C.S. Resident. Vacant 1st November.

Applications to Hospital Secretary.

NUNEATON. MANOR HOSPITAL. Senior House OFFICER in Anæsthetics. Resident or non-resident. Recognised D.A. and F.F.A. R.C.S. Vacant 20th November.

Applications to Hospital Secretary.

OXFORD REGIONAL HOSPITAL BOARD. Applications are invited for the new appointment of REGISTRAR to the Department of Geriatric Medicine at Battle Hospital, Oxford-road, Reading (at present 83 geriatric and 79 long-stay beds). Previous experience of modern geriatric methods is desirable. The appointment will be for 1 year, renewable for a further year. Single accommodation is available. The department, which has full diagnostic and therapeutic facilities, is under the charge of a Consultant Geriatrician and there is a resident Senior House Officer. Candidates may visit the Hospital by appointment.

Application forms, obtainable from the Secretary, Registrars Committee, 43, Banbury-road, Oxford, to be returned by 12th November, 1958.

OXFORD REGIONAL HOSPITAL BOARD. Applications are invited for the post of REGISTRAR in Obstetrics and Gynæcology to the hospitals of the Aylesbury area. It is hoped that this post may be interchangeable with the Departments of Obstetrics and Gynæcology, United Oxford Hospitals, after the first year. The appointment is for 1 year, eligible for extension to a second year.

Applications, on forms obtainable from the Secretary, Registrars Committee, 43, Banbury-road, Oxford, should reach him by 18th November, 1958.

OXFORD. UNITED OXFORD HOSPITALS/OXFORD REGIONAL HOSPITAL BOARD. 2 SENIOR REGISTRARS in General Surgery (*a*) 1 to the Radcliffe Infirmary, Oxford, and (*b*) 1 to Northampton General Hospital. These posts are included in the exchange scheme for Senior Registrars and the successful candidates will exchange duties after approximately 2 years. The appointments will be for 1 year in the first instance, eligible for extension to 4 years. Posts available 1st January, 1959.

Applications, on forms obtainable from the Joint Secretary, Senior Registrars Committee, must reach him by 11th November, 1958.

OXFORD. THE UNITED OXFORD HOSPITALS. Applications are invited for the post of HOUSE OFFICER in the Accident Service at the Radcliffe Infirmary for a period of 6 months, commencing as soon as possible.

Applications, on forms obtainable from the Administrator, Radcliffe Infirmary, Oxford, should be received not later than 22nd November, 1958.

OLDHAM AND DISTRICT HOSPITAL MANAGE-MENT COMMITTEE. Applications are invited for the appointment of Locum SENIOR HOUSE OFFICER (general surgery) vacant immediately, with duties at the Oldham Royal Infirmary and/or the Oldham and District General Hospital. The appointment will be tenable for a period of approximately 6 months.

Applications, quoting full particulars of qualifications and experience, together with the names and addresses of 2 referees, should be sent immediately to the Group Secretary, Central Offices, Rochdale-road, Oldham.

PAISLEY. RICCARTSBAR HOSPITAL. (344 Beds.) Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER at the above Hospital. The post can be resident or non-resident. Experience in all modern therapies is available; active outpatient clinics and opportunities for child guidance. The successful candidate would be given facilities to attend the postgraduate course at Glasgow University. The Hospital is recognised for various D.P.M.s.

Applications, giving full details of experience and the names of 2 referees, should be sent to the Physician-Superintendent within 2 weeks of the appearance of this advertisement.

PLYMOUTH, SOUTH DEVON AND EAST CORNWALL GENERAL HOSPITAL GROUP. SENIOR RESIDENT ANÆSTHETIST (Junior Hospital Medical Officer grade) for general anæsthetic duties in the Clinical Area. The post offers experience in anæsthesia for all grades of surgery.

Apply stating age, nationality, qualifications and experience, and giving names and addresses of 3 referees to the Group Secretary, 7, Nelson-gardens, Plymouth.

PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL.

HOUSE SURGEON, pre-registration post, vacant 1st December, 1958. Devonport Section.

HOUSE SURGEONS, pre-registration posts, vacancies, 2 on 1st January, 1959. Freedom Fields Section.

HOUSE SURGEONS, pre-registration posts, vacancies, 1 immediately, and 9th January, 1959. Greenbank-road Section.

All posts are recognised for the F.R.C.S.

Apply with names of 3 referees, also stating age, nationality, qualifications and experience to the Group Secretary, 7, Nelson-gardens, Plymouth.

PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL, Greenbank-road, PLYMOUTH. HOUSE PHYSICIANS, pre-registration posts, vacancies 1st and 14th January, 1959.

Apply with names of 3 referees, also stating age, nationality, qualifications and experience to the Group Secretary, 7, Nelson-gardens, Plymouth.

POOLE GENERAL HOSPITAL, Poole, Dorset. (320 Beds.) BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON (pre-registration) required for 17th November, 1958. Post recognised for F.R.C.S. and F.R.C.S. (Ed.).

Applications to the Hospital Secretary.

POOLE GENERAL HOSPITAL, Poole, Dorset. (320 Beds.) BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. HOUSE PHYSICIAN (pre-registration) required on 10th November, 1958.

Applications to the Hospital Secretary.

READING AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER (Area Accident and Orthopædic Department). Recognised for F.R.C.S. Duties include work in Area Casualty Department at Battle Hospital, Reading. Person appointed will work with Registrar and House Officer.

Apply, giving nationality, present post, and qualifications with dates, together with the names of 2 referees, to Group Secretary, 3, Craven-road, Reading.

READING AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR HOUSE OFFICER to the Department of Geriatric Medicine, which is being developed at Battle Hospital, Reading, under the charge of a Consultant Geriatric Physician.

Further particulars may be obtained from the Group Secretary, 3, Craven-road, Reading, to whom applications, stating age, qualifications and names of 3 referees, should be addressed.

READING COMBINED HOSPITALS. Area Department OF OBSTETRICS AND GYNÆCOLOGY. (100 Beds.) Applications invited from registered medical practitioners for resident post of HOUSE SURGEON. Post vacant 9th November, 1958, for 1 year. 6 months gynæcology at Royal Berkshire Hospital, and 6 months in Maternity Unit at Battle Hospital. Both appointments recognised for Diplomas of R.C.O.G.

Write, stating age, qualifications with dates, nationality and present post, with copy of recent testimonial, to Secretary, Royal Berkshire Hospital, Reading.

READING. ROYAL BERKSHIRE HOSPITAL. (397 Beds.) Applications are invited from registered and provisionally registered medical practitioners for 2 posts as RESIDENT HOUSE SURGEON, vacant 26th November and 1st December, 1958, and tenable for 6 months.

Write, stating age, qualifications with dates, nationality, present post, with copies of 2 recent testimonials, to Secretary.

READING. ROYAL BERKSHIRE HOSPITAL. (338 Beds.) Applications are invited from registered medical practitioners (Male or Female) for the post of RESIDENT SENIOR HOUSE OFFICER (anæsthetics). Vacant immediately for a period of 1 year. Post recognised for F.F.A. R.C.S.

Write, stating age, qualifications with dates, nationality and present post, together with names of 3 referees, to Group Secretary, Reading and District Hospital Management Committee, 3, Craven-road, Reading.

READING AREA DEPARTMENT OF MEDICINE. Applications are invited from registered and provisionally registered medical practitioners for 2 posts as RESIDENT HOUSE PHYSICIAN, vacant 1st December, 1958, for 6 months. Successful candidates required to carry out duties at the following Reading Hospitals: Royal Berkshire (397 Beds) and Prospect Park (104 Beds).

Write immediately, stating age, qualifications, with dates, nationality, present post, with copies of 2 recent testimonials, to Secretary, Royal Berkshire Hospital, Reading.

RICHMOND, SURREY. ROYAL HOSPITAL. Pre-registration HOUSE SURGEON (recognised for F.R.C.S.) required 16th November, 1958, for busy acute general hospital of 121 Beds with full consultant staff.

Applications invited immediately (acceptable in advance of examination results), giving age, qualifications, and names of 2 referees, to Administrative Officer.

RICHMOND, SURREY. ROYAL HOSPITAL. Pre-registration HOUSE PHYSICIAN required immediately for busy acute general hospital of 121 Beds with full consultant staff.

Applications invited immediately (acceptable in advance of examination results), giving age, qualifications, and names of 2 referees, to Administrative Officer.

ROCHESTER, KENT. ST. BARTHOLOMEW'S HOSPITAL. MEDWAY AND GRAVESEND HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE SURGEON (orthopædics) required. Post vacant now and tenable for 1 year. Recognised for the F.R.C.S. and providing excellent experience. Salary £819 10s., less £150 p.a. for residential emoluments.

Applications, stating age, qualifications, experience and nationality, with recent testimonials, to Hospital Secretary.

ROCHESTER, KENT. ST. BARTHOLOMEW'S HOSPITAL. MEDWAY AND GRAVESEND HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the pre-registration post of HOUSE SURGEON in General Surgery, vacant towards end of November. Approved for F.R.C.S. Salary scale £467 10s.–£577 10s. p.a. according to experience.

Applications, stating age, qualifications, experience and nationality, to the Hospital Secretary.

ROCHFORD, ESSEX. GENERAL HOSPITAL. (622 Beds.) SENIOR HOUSE OFFICER required for Geriatric Unit at the above Hospital. Post vacant early November. A wide range of facilities are available for the investigation, treatment, and rehabilitation of acute and chronic inpatients and outpatients.

Applications, stating, age, &c., to be sent to the Secretary as soon as possible.

ROMFORD, ESSEX. OLDCHURCH HOSPITAL. (722 Beds.) ORTHOPÆDIC HOUSE SURGEON (resident) required in the Orthopædic and Accident Unit. The service consists of 100 Beds equally divided between traumatic surgery and "cold" orthopædics. Post is recognised for pre-registration purposes and for F.R.C.S.

Applications to be sent to Group Secretary, Romford Hospital Management Committee, Oldchurch Hospital, as soon as possible.

ROMFORD, ESSEX. OLDCHURCH HOSPITAL. (722 Beds.) RESIDENT HOUSE SURGEONS (2) required in the General Surgical Unit. Recognised for F.R.C.S. Open to either pre-registration applicants or to fully registered practitioners. This very active Unit of a total of approximately 180 Beds affords ample opportunities for candidates to obtain first-class tuition and experience. The candidates appointed will be attached to a unit of approximately 60 Beds.

Apply immediately to Group Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital.

ROMFORD, ESSEX. OLDCHURCH HOSPITAL. (722 Beds.) RESIDENT HOUSE PHYSICIAN required from 3rd November, 1958. Open to either pre-registration applicants or to fully registered practitioners.

Apply immediately to Group Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital.

ROMFORD, ESSEX. VICTORIA HOSPITAL. (99 Beds.) RESIDENT HOUSE PHYSICIAN (Male) required immediately. (Not pre-registration appointment.)

Applications should be forwarded to the Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

ROTHERHAM HOSPITAL, Doncaster Gate, Rotherham. (161 Beds. Recognised for F.R.C.S. examination.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT REGISTRAR (orthopædics and casualty) required immediately. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 10th November, 1958, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

SALFORD. LADYWELL HOSPITAL. (Chest Unit, 110 Beds.) SALFORD HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the resident post of JUNIOR HOSPITAL MEDICAL OFFICER at the above Hospital. The post is tenable for a maximum period of 4 years. Previous experience in the treatment of pulmonary tuberculosis is desirable. There is a visiting Thoracic Surgeon, and the surgery is undertaken at Baguley Hospital, Manchester, which is nearby.

Applications, stating age, qualifications and experience, together with the names of 2 referees, should be submitted immediately to the Hospital Secretary, Ladywell Hospital, Salford, 5, Lancs.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the following appointments, which will be for 1 year in the first instance:—

SENIOR REGISTRAR in Anæsthetics based at the Royal Infirmary, Glasgow.

SENIOR REGISTRAR in Medicine based at the Victoria Infirmary, Glasgow.

Applications (12 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, by 15th November, 1958.

SCOTLAND. EASTERN REGIONAL HOSPITAL BOARD. Dundee Area. Thoracic (and cardiac) surgery. Applications are invited for the appointment of SENIOR REGISTRAR or REGISTRAR in Surgery (depending upon qualifications and experience) for duty in the Regional Thoracic Surgical Centre at Ashludie Hospital, Monifieth, by Dundee (222 Beds—60 for thoracic surgery), and in the Cardiovascular Department of the Professorial Surgical Unit at Dundee Royal Infirmary (the principal general teaching hospital associated with the University of St. Andrews—557 Beds). Previous experience in thoracic surgery and general chest medicine an advantage. Salary and conditions of service in accordance with national agreement.

Further particulars and forms of application from the Secretary to the Board, 430, Blackness-road, Dundee, with whom applications must be lodged not later than 7th November, 1958.

SEDGEFIELD GENERAL HOSPITAL, Sedgefield, Stockton-on-Tees. (336 Beds.) SENIOR HOUSE OFFICER ANÆSTHETIST required. Married accommodation available. Full Consultant Staff employed. Post is recognised in connection with higher examinations and there is a good medical library.

Applications to the Group Secretary, North Tee-side Hospital Management Committee, at the above address as soon as possible.

SHEFFIELD, 6. KING EDWARD VII ORTHOPÆDIC HOSPITAL, Rivelin Valley-road. SHEFFIELD NO. 3 HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of a SENIOR HOUSE OFFICER. The Hospital has 154 Beds, 100 of which are occupied by children. It has a modern unit for the treatment of poliomyelitis and has close contact with a nearby infectious diseases hospital. The post would suit applicants interested in children's diseases as there is a fair amount of general medical work. A non-resident appointment might be considered.

Applications, with names of 2 referees, to the Group Secretary, Sheffield No. 3 Hospital Management Committee, Lodge Moor Hospital, Sheffield, 10.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. ROYAL HOSPITAL. Applications invited for the post of REGISTRAR or SENIOR HOUSE OFFICER to the Department of Neurology. Post vacant 15th December, 1958. This is a large Neurological Department in a Teaching Hospital Group. Post offers wide experience and opportunities for postgraduate training and for attending postgraduate teaching in other departments.

Applications, stating age, qualifications and experience, with the names of 3 referees, should be sent not later than 11th November, 1958, to Chief Administrative Officer, United Sheffield Hospitals, West-street, Sheffield, 1.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. ROYAL INFIRMARY. Applications invited for the posts of REGISTRAR and SENIOR HOUSE OFFICER in the Rupert Hallam Department of Dermatology at the above Hospital.

Applications, stating age, qualifications and experience, with the names of 3 referees, should be sent to the Chief Administrative Officer, United Sheffield Hospitals, West-street, Sheffield, 1, not later than 11th November, 1958.

SHOREHAM-BY-SEA, SUSSEX. SOUTHLANDS HOSPITAL. Applications are invited for the appointment of RESIDENT HOUSE PHYSICIAN/HOUSE SURGEON to run consecutively for a period of 6 months in each post. Posts approved for pre- or post-registration practitioners and F.R.C.S.

Applications to Hospital Secretary, Southlands Hospital, Shoreham-by-Sea. A. V. OAKTON, Group Secretary, Worthing Group Hospital Management Committee.

SOUTHALL, MIDDLESEX. ST. BERNARD'S HOSPITAL FOR NERVOUS AND MENTAL DISORDERS. SENIOR HOUSE OFFICER required. Facilities are offered junior staff to become versed in all branches of psychiatry. National Health Service salary and conditions.

Applications, giving full details and copies of 3 recent testimonials, should be sent to the Physician-Superintendent within 14 days of the appearance of this advertisement.

SHREWSBURY. ROYAL SALOP INFIRMARY. (241 Beds.) SENIOR HOUSE OFFICER (casualty) (1 of 2). Resident. Mornings 9 A.M. to 1 P.M., alternate afternoons with evenings and alternate weekends off duty. Post recognised for F.R.C.S. Vacant 14th November, 1958.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. ROYAL SALOP INFIRMARY. (216 Beds.) 2 HOUSE SURGEONS. Vacant immediately. Pre-registration candidates eligible. Recognised for the F.R.C.S.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. ROYAL SALOP INFIRMARY. Orthopædic/Accident HOUSE SURGEON (Senior House Officer). Successful applicant will be allowed to attend for 2 days a month at the Robert Jones and Agnes Hunt Orthopædic Hospital, Oswestry, for postgraduate study, with the Consultant. Post recognised under revised Fellowship regulations in respect of 6 months' training required for the Final Fellowship examination. Vacant immediately.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. ROYAL SALOP INFIRMARY/COPTHORNE HOSPITAL. (500 Beds.) HOUSE PHYSICIAN. Pre-registration candidates eligible. Vacant immediately.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. ROYAL SALOP INFIRMARY/COPTHORNE HOSPITAL. (500 Beds.) Senior House Officer to work as CLINICAL PATHOLOGIST to Group Laboratory. Appointment tenable for 1 year, resident or non-resident. Recognised for Diploma in Pathology. Vacant 1st January, 1959. A Unit of the Public Health Laboratory service is housed in the same building and there are facilities for training in all the 4 main branches of pathology.

Applications to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury, naming 3 referees.

SHREWSBURY. EYE, EAR AND THROAT HOSPITAL. SENIOR HOUSE OFFICER (E.N.T.) Duties at E.N.T. Hospital (68 Beds) and Copthorne Hospital (168 Beds). Post recognised for the D.L.O. and F.R.C.S. Vacant 29th November, 1958.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SLOUGH, BUCKINGHAMSHIRE. UPTON HOSPITAL. Locum SENIOR SURGICAL REGISTRAR required 17th–29th November inclusive.

Applications, with names of 2 referees, to Secretary.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL. (274 Beds. Recognised for F.R.C.S.) CASUALTY OFFICER (Senior House Officer grading) required.

Applications, with copies of testimonials, to be submitted as soon as possible to the Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL. (274 Beds. Recognised for F.R.C.S.) ORTHOPÆDIC HOUSE SURGEON (pre-registration candidates eligible). Post offers excellent experience in the treatment of traumatic conditions.

Applications to Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHEND. GENERAL HOSPITAL. (262 Beds.) Applications are invited for appointment as HOUSE SURGEON (pre-registration). Post vacant 17th December, 1958.

Applications, stating age, qualifications and previous experience, with copies of recent testimonials (1 testimonial sufficient from applicants for first appointment), should reach the undersigned by 6th November, 1958.

J. C. FIELD, Secretary.

SOUTHEND. GENERAL HOSPITAL. (262 Beds.) Applications are invited for appointment as HOUSE PHYSICIAN (pre-registration). Post vacant 17th December, 1958.

Applications, stating age, qualifications and previous experience, with copies of recent testimonials (1 testimonial sufficient from applicants for first appointment), should reach the undersigned by 6th November, 1958.

J. C. FIELD, Secretary.

ST. ALBANS CITY HOSPITAL. (384 Beds.) North West METROPOLITAN REGIONAL HOSPITAL BOARD. Whole-time MEDICAL REGISTRAR required. Post vacant approximately 14th January, 1959. Preference given to candidates having considerable experience in dealing with medical emergencies. Hospital may be visited by direct appointment.

Application forms obtainable from and returnable to Secretary, Mid-Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans, by 15th November, 1958.

ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire. (384 Beds.) HOUSE PHYSICIAN (House Officer grade) required for 1 of the 2 medical teams. Post vacant 18th November, 1958, and tenable for 6 months. Preference given to candidates seeking post under the Medical Act, 1950.

Applications to Secretary, Mid-Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans.

ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire. (384 Beds.) HOUSE PHYSICIAN (House Officer grade) required for duties mainly in the Pædiatric Department. Preference given to candidates seeking pre-registration post under the Medical Act, 1950.

Applications to Secretary, Mid-Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans.

ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire (384 Beds.) Locum Tenens GYNÆCOLOGICAL AND OBSTETRIC REGISTRAR, resident, required for the period 1st–13th December, 1958.

Applications to Secretary, Mid-Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans.

ST. ALBANS, HERTFORDSHIRE. NAPSBURY MENTAL HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER, appointment to commence immediately. Previous experience as House Physician or House Surgeon essential. Previous psychiatric experience desirable but not essential. Regular clinical case conferences, good psychiatric library and other training facilities. Salary £819 10s. p.a. Single accommodation is available, if required, for which a charge will be made.

Applications, with references or testimonials, to be sent not later than 11th November, 1958, to the Medical Superintendent (telephone: Bowmansgreen 3333).

STIRLING AND CLACKMANNAN HOSPITALS BOARD OF MANAGEMENT AND NATIONAL HEALTH SERVICE EXECUTIVE COUNCIL FOR THE COUNTIES OF STIRLING AND CLACKMANNAN. Applications are invited for 2 joint appointments as SENIOR HOUSE OFFICER in Surgery at Clackmannan County Hospital and TRAINEE GENERAL PRACTITIONER in the Alloa area. The appointments will be for 2 years and the successful applicants will spend a total of 1 year at Clackmannan County Hospital and 1 year as a Trainee General Practitioner with a selected principal. The salary for the post will be £819 10s. for the first year, and £850 for the second year. A car allowance may be payable in addition. Married accommodation will be available.

Applications, with names of 2 referees, should be sent to the Group Medical Superintendent, Royal Infirmary, Stirling.

STIRLING AND CLACKMANNAN HOSPITALS BOARD OF MANAGEMENT. Applications are invited for the post of RESIDENT HOUSE SURGEON (pre-registration) at Clackmannan County Hospital. The post is now vacant.

Applications should be sent immediately to the Group Medical Superintendent, Stirling Royal Infirmary.

STOCKPORT INFIRMARY. (163 Beds.) Applications are invited for the post of HOUSE OFFICER (general surgery) vacant 2nd November, 1958. This is an approved pre-registration post and is recognised for the F.R.C.S.

Applications, with copies of 2 testimonials, to the Group Secretary, Stockport and Buxton Hospital Management Committee, 59B, Shaw Heath, Stockport.

STOCKPORT INFIRMARY. (163 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (Assistant Resident Surgical Officer) (general and orthopædics). Vacant now. The post is recognised for the F.R.C.S.

Applications, stating age, experience and qualifications, together with copies of 2 testimonials, to be addressed to the Secretary, Stockport and Buxton Hospital Management Committee, 59B, Shaw Heath, Stockport.

STOCKPORT. STEPPING HILL HOSPITAL. (529 Beds.) Applications are invited for the pre-registration post of HOUSE OFFICER (surgery).

Applications, with full particulars and copies of 2 testimonials, to the Secretary, Stockport and Buxton Hospital Management Committee, 59B, Shaw Heath, Stockport.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. Whole-time Locum Tenens SENIOR REGISTRAR in Obstetrics and Gynæcology. Vacant immediately for approximately 3 months.

Apply to Secretary, Regional Hospital Board, 10, Augustus-road, Birmingham, 15, naming 3 referees and giving details of previous experience.

STOKE-ON-TRENT (near). GROUNDSLOW HOSPITAL, TITTENSOR, near STOKE-ON-TRENT. Pre-registration or third HOUSE OFFICER post in Obstetrics and Gynæcology. Now vacant.

Applications, with details of qualifications and names for reference, to Group Secretary, Stafford Hospital Management Committee, 13, Foregate-street, Stafford.

SUNDERLAND AREA HOSPITAL MANAGEMENT COMMITTEE. Department of Medicine and Geriatrics. SENIOR HOUSE OFFICER or HOUSE OFFICER required immediately for the above Unit which has a total of 490 Beds (217 acute). Grade according to experience. Consultant Physician-in-charge. First-class experience afforded, good prospects of promotion, and excellent opportunities for studying for membership examination and research. Salary and conditions of service according to Whitley Council recommendations.

Apply, giving full details of qualifications and experience and naming 2 referees, to Hospital Secretary, General Hospital, Chester-road, Sunderland.

SWANSEA HOSPITAL, Swansea. (413 Beds.) Glantawe HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the resident post of SENIOR HOUSE OFFICER in the Traumatic and Orthopædic Department of the above Hospital. Vacancy 1st January, 1959. The post is recognised under the F.R.C.S. regulations for 6 months' casualty training. It offers exceptional experience in all aspects of traumatic surgery as occurring in a large industrial centre and port.

Applications, stating age and experience, together with copies of 2 recent testimonials, should be forwarded to the Hospital Secretary by 8th November, 1958.

T. E. JONES, Group Secretary.

SWANSEA HOSPITAL, Swansea. (413 Beds.) Glantawe HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the resident post of SENIOR HOUSE OFFICER in the E.N.T. Department of the above Hospital. Vacancy 27th December, 1958. The Hospital is recognised under the regulations for the F.R.C.S. (E.N.T.) and the D.L.O.

Applications, stating age, qualifications and experience, together with the names of 2 referees, should be forwarded to the Hospital Secretary by 8th November, 1958.

T. E. JONES, Group Secretary.

SWANSEA HOSPITAL, Swansea. (413 Beds.) Glantawe HOSPITAL MANAGEMENT COMMITTEE. Registered medical practitioners are invited to apply for the resident appointment of SENIOR HOUSE OFFICER in the Ophthalmic Department of the above Hospital. Vacancy 1st December, 1958. The post is recognised for the F.R.C.S.(Eng.) and D.O. examinations.

Applications, stating age, qualifications and experience, together with copies of 2 recent testimonials, should be addressed to the Hospital Secretary. T. E. JONES, Group Secretary.

TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS MEMORIAL HOSPITAL. HOUSE SURGEON required for the Unit of Obstetrics and Gynæcology. Post recognised for M.R.C.O.G., vacant 22nd December. Pre-registration post.

Applications, with copies of 2 testimonials, to Secretary.

TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS MEMORIAL HOSPITAL. SENIOR HOUSE OFFICER (anæsthetics) required 1st December. Post, which is tenable for 1 year, will be resident.

Applications, with 2 recent testimonials, to Secretary.

TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS MEMORIAL HOSPITAL. HOUSE SURGEON required for post vacant 22nd December. Pre-registration post.

Applications, stating age, qualifications (with dates), with copies of 2 testimonials, to Secretary.

TILBURY AND RIVERSIDE GENERAL HOSPITAL, ORSETT BRANCH, ORSETT, ESSEX. Applications are invited for the post of RESIDENT ORTHOPÆDIC HOUSE SURGEON at the above Hospital. The post is recognised under the Medical Act for pre-registration purposes, and suitable candidates are invited to apply. There exists a new Casualty Reception Unit at this Hospital. The appointment, which becomes vacant immediately, is for 6 months in the first instance.

Applications, together with copies of recent testimonials, should be forwarded to the undersigned.

G. E. WHYTE, Group Secretary,
Thurrock Hospital, Tilbury and South East Essex
Grays, Essex. Hospital Management Committee.

TORQUAY. TORBAY HOSPITAL. (180 acute general beds.) HOUSE OFFICER (medicine), Male or Female, required for last week of November. Pre-registration appointment. General duties which will include some work in the E.N.T., the Ophthalmic, and Radiotherapy Departments.

Applications, stating qualifications, nationality, age, together with copy testimonials (quoting reference F.955/91), to the Group Secretary, Torquay District Hospital Management Committee, Torbay Hospital, Torquay, S. Devon.

TAUNTON AND SOMERSET HOSPITAL, Taunton, SOMERSET. SENIOR HOUSE OFFICER (anæsthetics) required. Post, vacant early December, is recognised for F.F.A. R.C.S. and D.A. A Registrar in Anæsthetics is also employed in the South Somerset Clinical Area, in which the above is the principal General Hospital.

Applications, stating age, nationality, experience in anæsthetics (if any), together with the names of 2 referees, to the Group Secretary, Taunton Hospital Management Committee, Musgrove Park Hospital, Taunton.

TAUNTON AND SOMERSET HOSPITAL, Taunton, SOMERSET. Applications are invited for the post of SENIOR HOUSE OFFICER (casualty and orthopædic).

Applications, stating age, nationality and qualifications, together with the names of 2 referees, should be forwarded to the Group Secretary, Taunton Hospital Management Committee, Musgrove Park Hospital, Taunton.

TUNBRIDGE WELLS (near). PEMBURY HOSPITAL, PEMBURY. (357 staffed available beds.) TUNBRIDGE WELLS GROUP HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (obstetrics and gynæcology). Applications invited for this appointment, which is a combined appointment of 1 year in obstetrics gynæcology, recognised for M.R.C.O.G. Vacant 1st December, 1958. There are 66 obstetric beds and 20 gynæcological beds. Applicants must have held a previous obstetric post.

Apply, stating age, qualifications and experience, with 2 recent testimonials, by 16th November, 1958, to Group Secretary, Sherwood Park, Pembury-road, Tunbridge Wells.

WATFORD HOSPITAL UNIT. (560 Beds.) Applications are invited for the post of HOUSE SURGEON, pre- or post-registration. Post recognised for F.R.C.S. General surgical unit 100 Beds. 2 surgical teams. Residency at Peace Memorial Hospital. Salary according to National Health Service scale.

Please send applications, with copies of recent testimonials, to the Administrator, Peace Memorial Hospital, Watford, Herts.

WATFORD. PEACE MEMORIAL HOSPITAL. North WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR in Pathology (non-resident) required in the Department of Morbid Anatomy at the Group Laboratory at above Hospital. Previous experience essential. Post vacant immediately. Laboratory may be visited by direct appointment.

Application forms obtainable from, and returnable to, Secretary, West Herts Group Hospital Management Committee, 9, Rickmansworth-road, Watford, Herts, by not later than 11th November, 1958.

WATFORD PEACE MEMORIAL HOSPITAL, Watford, HERTFORDSHIRE. (211 Beds.) CASUALTY OFFICER (Senior House Officer) required. Modern department employing 4 full-time Casualty Officers, including whole-time Surgeon-in-charge. Post recognised for F.R.C.S. Resident or non-resident. Post vacant 11th December.

Please send applications, with copies of 2 recent testimonials, to the Administrator.

WAKEFIELD. PINDERFIELDS GENERAL HOSPITAL. REGIONAL THORACIC CENTRE. Applications invited for positions of SENIOR HOUSE PHYSICIAN and SENIOR HOUSE SURGEON. Salary £819 10s. p.a. £150 p.a. charged for accommodation.

Address written applications, giving full personal particulars, details of experience, and 2 names and addresses for reference, to W. BOWRING, Group Secretary, Pinderfields General Hospital, Wakefield.

WAKEFIELD. PINDERFIELDS GENERAL HOSPITAL. REGIONAL THORACIC CENTRE. Applications invited for position of JUNIOR HOSPITAL MEDICAL OFFICER. Salary scale £852 10s.–£55–£1182 10s. p.a. £170 p.a. charged for accommodation.

Address written applications, giving full personal particulars, details of experience and 2 names and addresses for reference, to W. BOWRING, Group Secretary, Pinderfields General Hospital, Wakefield.

WELSH REGIONAL HOSPITAL BOARD.

REGISTRAR (pædiatrics), based Merthyr General Hospital, Merthyr, to serve Merthyr and Aberdare Hospital Management Committee.

REGISTRAR in Radiotherapy, Whitchurch Hospital, Whitchurch, Glamorgan. Duties will include visits to United Cardiff Hospitals. Non-resident. Vacant 14th December, 1958.

REGISTRAR (plastic surgery), St. Lawrence Hospital, Chepstow (182 Beds). Expected to visit other hospitals in South Wales area. Considerable opportunities for training in specialty. Accommodation for single person.

REGISTRAR (general surgery), Caernarvon and Anglesey General Hospital, Bangor (130 Beds). Non-resident. Hospital recognised for F.R.C.S.

REGISTRAR (psychiatry), St. David's Hospital, Carmarthen (1000 Beds). All modern forms of treatment carried out. Extensive outpatient service undertaken. Hospital recognised for training for D.P.M. Flat available. Vacant 1st January, 1959.

Subject to review end of first year.

Application forms from Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 14 days.

WELSH REGIONAL BUREAU FOR PRE-REGISTRATION HOSPITAL APPOINTMENTS

It is anticipated that the following Pre-registration HOUSE OFFICER posts at the under-mentioned hospitals in the Welsh Region will be vacant on the dates given. These posts have been approved by the Licensing Body for the employment of medical students who, after passing their qualifying examinations, are required to spend a prescribed period in approved hospitals before they become eligible for full registration as medical practitioners.

Application forms may be obtained from the Regional Bureau, Welsh National School of Medicine, 34, Newport-road, Cardiff, Wales, and should be returned not later than noon on Friday, 5th December, 1958.

Newport and East Monmouthshire

ROYAL GWENT, NEWPORT, MON. (264 Beds)
2 medical (1 includes some pædiatrics)—1st February, 1959.
3 surgical—1st February, 1959. Post recognised for F.R.C.S.
1 gynæcological (surgical)—1st February, 1959.

ST. WOOLOS, NEWPORT, MON. (379 Beds)
2 medical (1 includes some tuberculosis; 1 includes some geriatrics)—1st February, 1959.
1 surgical—1st February, 1959. Post recognised for F.R.C.S.
1 pædiatric—1st February, 1959. Post recognised for D.C.H.

PONTYPOOL AND DISTRICT, PONTYPOOL, MON. (126 Beds)
1 medical (includes some pædiatrics)—1st February, 1959.
1 surgical—1st February, 1959. Post recognised for F.R.C.S.

Rhymney and Sirhowy Valleys

CAERPHILLY DISTRICT MINERS', CAERPHILLY, GLAM. (198 Beds) (Married quarters may be available)
1 medical—1st February, 1959.
2 surgical (1 with duties in Orthopædic Department)—1st February, 1959.

TREDEGAR GENERAL, TREDEGAR, MON. (56 Beds). (Married quarters available)
1 surgical—1st February, 1959.

ST. JAMES, TREDEGAR, MON. (160 Beds). (Married quarters available)
1 midwifery—1st February, 1959.

Cardiff

ST. DAVID'S, CARDIFF, GLAM. (536 Beds)
3 medical—1st February, 1959.
1 orthopædic (surgical)—1st February, 1959.
1 pædiatric (medical)—1st February, 1959.
1 midwifery—1st February, 1959.

ROYAL HAMADRYAD GENERAL AND SEAMEN'S HOSPITAL, CARDIFF (66 Beds)
1 surgical (interchangeable with the post of genitourinary (surgical) at the Cardiff Royal Infirmary)—1st February, 1959.

Merthyr and Aberdare

MERTHYR GENERAL, MERTHYR TYDFIL, GLAM. (120 Beds)
1 medical—1st February, 1959.
1 surgical—1st February, 1959.

ST. TYDFIL'S, MERTHYR TYDFIL, GLAM. (375 Beds)
1 medical—1st February, 1959.
1 surgical—1st February, 1959.

Pontypridd and Rhondda

EAST GLAMORGAN, CHURCH VILLAGE, NEAR PONTYPRIDD, GLAM. (336 Beds)
2 medical—1st February, 1959.
2 surgical—1st February, 1959.
2 orthopædic (surgical)—1st February, 1959.
2 midwifery—1st February, 1959.
1 pædiatric (medical)—1st February, 1959.

Mid Glamorgan

BRIDGEND GENERAL, BRIDGEND, GLAM. (381 Beds)
2 medical—1st February, 1959.
2 surgical—1st February, 1959.
1 midwifery—1st February, 1959.

NEATH GENERAL, NEATH, GLAM. (412 Beds)
2 medical—1st February, 1959.
2 surgical—1st February, 1959.
1 midwifery—1st February, 1959.

Glantawe

SWANSEA GENERAL, SWANSEA, GLAM. (412 Beds)
2 medical—1st February, 1959.
2 surgical—1st February, 1959.

MORRISTON HOSPITAL, MORRISTON, NEAR SWANSEA, GLAM. (501 Beds)
2 medical—1st February, 1959.
3 surgical—1st February, 1959.
1 pædiatric (medical)—1st February, 1959.
1 orthopædic (surgical)—1st February, 1959.

LLANELLY HOSPITAL, LLANELLY, CARMS. (162 Beds)
1 medical—1st February, 1959.
2 surgical—1st February, 1959.

West Wales

WEST WALES GENERAL, CARMARTHEN. (188 Beds)
1 medical—1st February, 1959.
1 surgical—1st February, 1959.

PEMBROKE COUNTY WAR MEMORIAL, HAVERFORDWEST, PEMBS. (163 Beds)
1 medical—1st February, 1959.
1 surgical—1st February, 1959.

Mid Wales

ABERYSTWYTH GENERAL, ABERYSTWYTH. (90 Beds)
1 medical—1st February, 1959.
1 surgical—1st February, 1959.

Caernarvon and Anglesey

CAERNARVON AND ANGLESEY GENERAL, BANGOR, CAERNS. (130 Beds)
2 medical—1st February, 1959.
2 surgical—1st February, 1959.

LLANDUDNO GENERAL, LLANDUDNO, CAERNS. (134 Beds)
1 medical—1st February, 1959.
2 surgical—1st February, 1959.

ST. DAVID'S BANGOR (136 Beds)
1 midwifery—1st February, 1959.

Clwyd and Deeside

ROYAL ALEXANDRA, RHYL, FLINTS. (108 Beds)
1 medical—1st February, 1959.
1 medical (including pædiatrics)—Immediate vacancy.

ST. ASAPH GENERAL, ST. ASAPH, FLINTS. (198 Beds)
1 midwifery—1st February, 1959.

Wrexham, Powys and Mawddach

MAELOR GENERAL, WREXHAM (591 Beds)
2 medical—1st February, 1959.
3 surgical—1st February, 1959.
1 pædiatric (medical)—1st February, 1959.

WREXHAM WAR MEMORIAL, WREXHAM, DENBS. (230 Beds)
1 medical—1st February, 1959.
1 surgical—1st February, 1959.
1 orthopædic (surgical)—1st February, 1959.

WALSALL HOSPITAL MANAGEMENT COMMITTEE. Locum SENIOR HOUSE OFFICER (general surgery) required for the Walsall General (Sister Dora) Hospital.

Apply Group Secretary, Walsall General (Sister Dora) Hospital.

WESTON-SUPER-MARE GENERAL HOSPITAL. (104 Beds.) Applications are invited from duly qualified medical practitioners for the pre-registration appointment of HOUSE PHYSICIAN. Single residential accommodation provided. Vacant January, 1959.

Applications, stating age, qualifications, together with names and addresses of 2 referees, should be addressed to the Group Secretary, Weston-super-Mare Hospital Management Committee.

WICKFORD (near), ESSEX. RUNWELL HOSPITAL. (1052 Beds.) SENIOR HOUSE OFFICER (Male or Female) required for one of the Consultant's division and to assist in out-patient work. Excellent postgraduate facilities for D.P.M. Salary £819 10s. p.a., residential charge £150.

Applications, with copies of testimonials, to the Secretary.

WIGAN. ROYAL ALBERT EDWARD INFIRMARY. (200 Beds.) SENIOR HOUSE OFFICER in Orthopædic Surgery.

Applications to Secretary, Royal Albert Edward Infirmary, Wigan.

WINCHESTER. ROYAL HAMPSHIRE COUNTY HOSPITAL. (324 Beds.) HOUSE OFFICER (anæsthetics). Post vacant 1st January, 1959. The Hospital is recognised for the F.F.A. R.C.S. and D.A.

Applications, with copies of 2 testimonials, to the Hospital Secretary.

WINCHESTER. ROYAL HAMPSHIRE COUNTY HOSPITAL. (324 Beds.) HOUSE PHYSICIAN (obstetrics) required. Post recognised D.Obst.R.C.O.G. Vacant 1st January, 1959.

Applications, with copies of 2 testimonials, to the Hospital Secretary.

WINCHESTER. ROYAL HAMPSHIRE COUNTY HOSPITAL. (324 Beds.) HOUSE SURGEON (post recognised by Royal College of Surgeons) required for general surgery with some E.N.T. duties. Approved pre-registration post. Vacant 1st December.

Applications, with copies of 2 testimonials, to the Hospital Secretary.

WINCHESTER. ROYAL HAMPSHIRE COUNTY HOSPITAL. (324 Beds.) HOUSE PHYSICIAN (pre-registration). Vacant 1st January.

Applications, with copies of 2 testimonials, to the Hospital Secretary.

WINDSOR. KING EDWARD VII HOSPITAL. House SURGEON in General Surgery required, Male or Female, for post vacant 29th November. Recognised for F.R.C.S. Pre-registration post.

Applications, stating age, nationality, qualifications and copies of recent testimonials, to Secretary.

WINDSOR. KING EDWARD VII HOSPITAL. House SURGEON in General and Orthopædic Surgery required, Male or Female, for post vacant 16th November. Recognised for F.R.C.S. Pre-registration post.

Applications, stating age, nationality, qualifications, with dates, and copies of recent testimonials, to Secretary.

WOODFORD GREEN, ESSEX. HARTS HOSPITAL. (100 Beds.) SENIOR HOUSE OFFICER required. The Hospital is a modern sanatorium with Area Chest Clinic. The post offers exceptional opportunities for gaining experience in tuberculosis and diseases of the chest. Salary £819 10s. p.a., less £150 p.a. for board, lodging, &c., or married accommodation available if required.

Applications, with copies of 2 recent testimonials, should be sent immediately to Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

WORCESTER ROYAL INFIRMARY. House Surgeon (pre-registration or otherwise) required for General Surgery post at this busy general hospital of 213 Beds. The appointment offers wide and varied experience and is recognised for the F.R.C.S. examinations.

Applications to Hospital Secretary.

WORCESTER ROYAL INFIRMARY. House Surgeon (pre-registration or otherwise) required immediately for Orthopædic Department of this busy general hospital of 213 Beds. The appointment offers wide and varied experience.

Applications to Hospital Secretary.

WORKINGTON INFIRMARY, Cumberland. (174 Beds, pre-registration post, recognised F.R.C.S.(Ed.).) HOUSE SURGEON (first, second, or Senior House Officer post). Vacant beginning of November.

Detailed applications, with dates and names of 2 referees, to Group Secretary.

WREXHAM. MAELOR GENERAL HOSPITAL (591 Beds), WAR MEMORIAL HOSPITAL (230 Beds). Applications are invited for the posts of HOUSE SURGEONS (general surgery) now vacant. The posts are approved for pre-registration and for the F.R.C.S. examinations. Fully registered practitioners may apply.

Applications and testimonials to be sent to the Group Secretary, Wrexham, Powys and Mawddach Hospital Management Committee, Maelor General Hospital, Croesnewydd-road, Wrexham, North Wales.

WOLVERHAMPTON AND MIDLAND COUNTIES EYE INFIRMARY. SENIOR HOUSE OFFICER required. 100 Beds and busy Outpatient Department. Post vacant the middle of November. Recognised for F.R.C.S. and D.O. examinations.

Applications to Secretary, Eye Infirmary, Compton-road, Wolverhampton, as soon as possible.

WOLVERHAMPTON. THE ROYAL HOSPITAL. (An associated hospital of the Birmingham University Medical School.) Pre-registration HOUSE OFFICER (general surgery). Vacant immediately. Recognised for F.R.C.S.

Apply, with copies of 2 testimonials, to the Secretary.

WOLVERHAMPTON. THE ROYAL HOSPITAL. Senior HOUSE SURGEON for Thoracic Surgery and Casualty. Post recognised for F.R.C.S. Vacant immediately.

Apply, with 2 testimonials, to Secretary.

WOKING AND CHERTSEY GROUP LABORATORY. Applications invited for post of RESIDENT CLINICAL PATHOLOGIST (Senior House Officer). The post is one of 2, and involves a half share in emergency service. Training available in all branches of clinical pathology. Post tenable for 1 year. Salary £819 10s. p.a.

Applications, stating age, qualifications, &c., together with names of 2 referees, as soon as possible to the Director, Group Laboratory, St. Peter's Hospital, Chertsey, Surrey.

YORK. CLIFTON HOSPITAL. Junior Hospital Medical OFFICER required for above Mental Hospital (1208 Beds). Salary £852 10s. rising to £1182 10s. a year. Accommodation for single or married man.

Applications, with names of 3 referees, to Physician-Superintendent.

YORK. COUNTY HOSPITAL. (General—266 Beds.) Locum Tenens HOUSE PHYSICIAN required for 1 week from 17th November.

Applications, giving full particulars, and names of 2 referees, to Group Secretary, Bootham Park, York.

YORK. COUNTY HOSPITAL. (General—266 Beds.) Pre-registration HOUSE SURGEON required for the above Hospital. Post is vacant now and is tenable for 6 months.

Applications, giving names of 2 referees, to Group Secretary, York A and Tadcaster Hospital Management Committee, Bootham Park, York.

YORK MILITARY HOSPITAL (Civilian Wing). (60 Beds.) SENIOR HOUSE OFFICER required immediately. There are 30 general medical beds and 30 surgical beds. The Hospital is associated with the County Hospital, a general hospital with 266 Beds, where relief casualty and emergency work and relief work for House Surgeons may be undertaken and where residence can be provided. Applicants can be resident or non-resident.

Applications, stating age, nationality, experience, qualifications, and names of 2 referees, to Group Secretary, York A and Tadcaster Hospital Management Committee, Bootham Park, York.

CORK. SOUTH CHARITABLE INFIRMARY AND COUNTY HOSPITAL. The Committee of Management will, at their meeting to be held on Monday, 17th November, proceed to elect 1 MEDICAL and 1 SURGICAL REGISTRAR. Candidates must be at least 3 years qualified, and those holding a major degree will receive salary of £700 p.a. with board, lodging, and laundry. Candidates preparing for a major degree will receive salary of £600 p.a. with board, lodging, and laundry. In addition each Registrar will receive a subvention from University College, Cork, for acting as Clinical Tutor. The position will be tenable for a period of 1 year, renewable annually, up to a maximum period of 3 years.

Applications, with particulars and conditions of the positions, may be obtained from the undersigned, with whom applications with qualifications, testimonials, and certificate of birth must be lodged on or before Monday 10th November. Candidates must be members of a medical defence union.

E. LINEHAN, Secretary.

CANADA. REGINA GENERAL HOSPITAL, Regina, SASKATCHEWAN, CANADA. Applications are invited for JUNIOR ROTATING INTERNESHIP appointments in an 800-Bed general hospital, commencing 1st July, 1959. All services very active. Salary $125 per month with full maintenance, with bonus of $25 per month payable for satisfactory service.

Applications should be sent to Mr. C. E. BARTON, Acting Superintendent.

IBADAN, NIGERIA. UNIVERSITY COLLEGE HOSPITAL. CHILDREN'S DEPARTMENT. The Board of Management invite application from registered medical practitioners with the requisite postgraduate experience for appointment as SENIOR REGISTRAR in the above Teaching Hospital. The salary offered for the post is £1542 rising by 3 annual increments to £1722 p.a. In addition, an inducement addition of £300 p.a. is payable to an expatriate doctor. A higher qualification is considered necessary for the post of Senior Registrar, but candidates ineligible for this reason may be considered for the post of Registrar, for 1 tour, renewable for a second tour by mutual agreement at a salary of £1266 p.a. plus inducement allowance payable to an expatriate of £270 p.a., rising after 1 year to £1320 and £300 respectively. The Children's Department consists of a unit of 70 Beds for general pædiatrics and a neonatal unit of 18–20 Cots. The Department has its own Outpatient Department and research laboratories and is a full teaching unit. The opportunities for studying pædiatrics in the tropics are excellent. The appointment will be initially for 1 tour of 12 months, renewable, for subsequent tours, by mutual agreement. On satisfactory completion of the agreement a gratuity of £37 10s. will be paid for each completed term of 3 months' service. An outfit allowance of £60 is payable on first appointment. Partly furnished quarters are provided at a rental of 8½% of salary excluding inducement allowance, and an expatriate doctor appointed will be eligible for 7 days' leave on full pay for each completed month of service in Nigeria. A Nigerian doctor is eligible for 5 days' leave for each completed month of service. Free first-class passages are provided for expatriate doctors and their wives on first appointment, for vacation leave and on completion of the agreement. Free first-class passages to Nigeria will, in certain circumstances, be provided for non-expatriate doctors. Candidates will be eligible for children's allowances in accordance with existing regulations. Arrangements can be made to enable doctors to continue their National Health Service superannuation scheme contributions, and details of the revised salary and gratuity payable in such cases will accompany application forms.

Applications should be submitted not later than 24th November, 1958, on the appropriate forms, which will be forwarded, together with additional information on receipt of an addressed foolscap envelope by the Adviser on Staff Recruitment, London Office, University College Hospital, Ibadan, 57, Catherine-place, Palace-street, London, S.W.1.

IBADAN, NIGERIA. UNIVERSITY COLLEGE HOSPITAL. The Board of Management invite applications from medical practitioners with the requisite postgraduate experience for the post of REGISTRAR in Clinical Pathology. The salary offered is £1266, rising by 1 annual increment to £1320 p.a., plus an inducement addition payable to an expatriate Registrar of £270 p.a. during first year and £300 p.a. subsequently. The appointment will be initially for 1 tour of 12 months and will be renewable by mutual agreement for a second tour. On satisfactory completion of the agreement a gratuity of £37 10s. will be paid for each completed term of 3 months' service. An outfit allowance of £60 is payable on first appointment. Partly-furnished quarters are provided at a rental of 8½% of salary excluding inducement allowance, and an expatriate doctor appointed will be eligible for 7 days' leave on full pay for each completed month of service in Nigeria. A Nigerian doctor is eligible for 5 days' leave for each completed month of service. Free first-class passages are provided for expatriate doctors and their wives on first appointment and on completion of the agreement. Free first-class passages to Nigeria will, in certain circumstances, be provided for non-expatriate doctors. Free first-class passages will be provided for vacation leave. Candidates will be eligible for children's allowances in accordance with existing regulations. Arrangements can be made to enable doctors to continue their National Health Service Superannuation Scheme contributions, and details of the revised salary and gratuity payable in such cases will accompany application forms.

Applications should be submitted not later than 15th November, 1958, on the appropriate forms, which will be forwarded, together with additional information, on receipt of an addressed foolscap envelope by the Adviser on Staff Recruitment, London Office, University College Hospital, Ibadan, 57, Catherine-place, Palace-street, London, S.W.1.

MICHIGAN, U.S.A. OAKWOOD HOSPITAL, Dearborn, MICHIGAN. Applications are invited for 1- or 2-year approved GENERAL PRACTICE RESIDENCY in modern 234-Bed general hospital 10 miles from Detroit. Excellent facilities. Hospital approved for Exchange-Visitor programme. Beginning monthly salary $250 if single, $300 if married. Free housing.

Apply: Director.

ST. JOHN'S, NEWFOUNDLAND, CANADA. GENERAL HOSPITAL. (456 Beds.) Applications are invited for the post of RESIDENT ANÆSTHETIST. Salary $3600 p.a., less $660 for board, maintenance, &c. The post is recognised by the Royal College of Surgeons and Physicians in Canada. Previous experience in anæsthetics is desirable. Transportation to St. John's will be provided by the Hospital, and on completion of 12 months' satisfactory service return passage to the United Kingdom.

Applications, stating age, qualifications and experience, together with the names of 2 referees, should be sent immediately to Dr. E. WILSON, Superintendent, General Hospital, St. John's, Newfoundland, Canada.

WEST INDIES. UNIVERSITY COLLEGE HOSPITAL OF THE WEST INDIES. Applications are invited for the appointment of a REGISTRAR or SENIOR REGISTRAR who will be in charge of the Casualty Department at the above Teaching Hospital. The staff of the department consists of 6 House Officers, and all types of medical and surgical cases are seen. The successful candidate will be responsible for the overall operation of the department, and the duties will include care and treatment of the nursing staff and some teaching of medical students who are studying for the medical degrees of the University of London. The salary for the appointment will be within the scale £1000–£100–£1200 : £1300–£100–£1600 p.a., according to qualifications and experience. Unfurnished accommodation will be provided at a rental of 5% of salary, and return passages to and from the country of recruitment for 1 person only.

Further information may be obtained from the Hospital Manager and Secretary, University College of the West Indies, Mona, Jamaica, West Indies, to whom applications, stating age, nationality, details of qualifications and experience, together with the names and addresses of 3 referees, should be sent not later than 29th November, 1958.

Public Appointments

FACTORY DOCTORS. Factories Acts 1937 and 1948. The following appointments as Appointed Factory Doctor are vacant. Apply to Chief Inspector of Factories, 19, St. James's-square, London, S.W.1.

District	*County*	*Latest date for receipt of applications*
ROMFORD ..	ESSEX ..	.. 15TH NOVEMBER, 1958
KIDWELLY ..	CARMARTHEN	.. 15TH NOVEMBER, 1958

LONDON COUNTY COUNCIL. Otologist required for 1 session a month at Hammersmith School Treatment Centre, Milson-road, W.14, for the examination of deaf or partially deaf children. Fee £5 5s. a session of 1¼–2½ hours.

Applications invited from medical practitioners of consultant status. Forms obtainable from Medical Officer of Health (PH/D.1/2043), County Hall, S.E.1, and returnable by 10th November.

LONDON COUNTY COUNCIL. Applications invited from medical practitioners practising locally under National Health Service for the following appointments as VISITING MEDICAL OFFICER.

(1) Newington Lodge, Westmoreland-road, S.E.17. A large home for the elderly, infirm and chronic sick, and for homeless families (accommodation for 860). Remuneration £400 a year.

(2) Newington Hostel for mothers in work, Boyson-road, Walworth (accommodation for 30 mothers and 30 babies). Remuneration £70 a year.

Remuneration in both cases exclusive of fees receivable from Executive Council in respect of residents and residential staff who may be taken on National Health Service list. Particulars and application forms from Medical Officer of Health (PH/D.1/2071), County Hall, S.E.1, returnable by 10th November.

TREASURY MEDICAL SERVICE. Applications are invited from medical practitioners, practising in the districts detailed below, for appointment, in a part-time and mainly advisory capacity, as LOCAL TREASURY MEDICAL OFFICER for each of the places or groups of places shown. The town shown in parentheses after the place-names indicates the Head Post Office Area in which the place, or group of places, is situated. Successful applicants will be required to examine and report on the condition of certain Government Officers, teachers, candidates for appointment, &c., who may be referred to them from time to time; and to attend when summoned to an emergency case of accident or sudden illness occurring in a Government office in the neighbourhood. Fees for this work, and mileage allowance where necessary, will be paid on a scale agreed with the British Medical Association.

Intending applicants should write, within 14 days, to Treasury Medical Adviser, Treasury Chambers, Whitehall, S.W.1, for a form on which application may be made. Applicants should be not more than 60 years of age.

The places for which applications are invited are as follows:—

ENGLAND AND WALES

Tring (Berkhamsted).
Pile (Bristol).
Harlech (Portmadoc).
Hawarden (Chester).
Littleport (Ely).
Baldock (Hitchin).
Allendale (Hexham).
London, S.W.2 (London).
Swallowfield (Reading).
Horley (Redhill).
Swansea (Swansea).
Langton Green (Tunbridge Wells).
Mere and Zeals (Warminster).
Storrington (Worthing).
Kingston-on-Thames (Kingston-on-Thames).
London, N.12 (London).

SCOTLAND

Bo'ness (Bathgate).
Dumfries (Dumfries).
Laurencekirk (Montrose).

DERBYSHIRE COUNTY COUNCIL. County Health DEPARTMENT. SENIOR ASSISTANT MEDICAL OFFICER FOR MENTAL HEALTH. Applications invited from registered medical practitioners with D.P.H. and/or D.P.M. Recognition by Ministry of Education for ascertainment of subnormal children, and experience in mental health generally and ascertainment of handicapped essential. Salary £1210–£55 (5)–£50 (4)–£1685 p.a. The point of entry on the scale depending on experience. Car and subsistence allowances. Post superannuable.

Particulars and application forms obtainable from County Medical Officer, County Offices, Matlock, Derbyshire. Closing date 10th November, 1958. Canvassing disqualifies.

ISLE OF WIGHT COUNTY COUNCIL. Appointment of Assistant County Medical Officer and District Medical Officer. Applications invited from duly qualified medical practitioners holding D.P.H. or similar qualification for whole-time appointment of ASSISTANT COUNTY MEDICAL OFFICER AND MEDICAL OFFICER OF HEALTH to the Borough of Ryde and the Urban Districts of Sandown Shanklin and Ventnor. County Council duties (65% of whole-time) mainly in connection with School Medical Services and the care of mothers and young children. D.C.H. preferred. District Council duties 35%. Salary on scale £1418 7s. 6d.–£56 2s. 6d. (3)–£59 16s. 3d. (1)–£40 11s. 3d. (4)–£1808 16s. 3d. Car allowance. Conditions negotiated by Medical Whitley Council "C" apply. Medical examination. Post superannuable.

Applications, stating age, qualifications, experience, names of 2 referees, and accompanied by copy of 1 recent testimonial, must reach the Clerk of the County Council, County Hall, Newport, I.W., not later than 10th November, 1958. Canvassing disqualifies.

MANCHESTER. CITY OF MANCHESTER HEALTH DEPARTMENT. Applications are invited from registered medical practitioners (Male or Female) for the position of MEDICAL OFFICER (maternity and child welfare) on the permanent staff. Applicants should have obstetric and pædiatric experience, and possession of the D.Obst.R.C.O.G., D.P.H., or D.C.H. will be an advantage. Duties principally in Maternity and Child Welfare Clinics. Salary scale £1050–£1475 p.a., the commencing salary depending on previous experience. Medical Council C conditions of service.

Application forms may be obtained from the Town Clerk, Town Hall, Manchester, 2, to whom they should be returned within 21 days of the appearance of this advertisement.

NATIONAL COAL BOARD. North Eastern Division. Require a registered medical practitioner for the post of MEDICAL OFFICER, to be responsible for the Divisional Radiological Service. Contact with industrial medicine involved and colliery visits necessary. Previous experience of chest disease or radiology an advantage, though training in the diagnosis of industrial pulmonary disease will be given. Salary £1600–£2400 with superannuation.

Apply, stating full details, including age, present post and salary, and giving names of 2 referees, to Divisional Chief Staff Officer, Holmwood House, Ecclesall-road South, Sheffield, 11, by 10th November. Mark envelopes "Staff Vacancy" and quote AA/407.

WEST BROMWICH. COUNTY BOROUGH OF WEST BROMWICH. HEALTH DEPARTMENT. Applications are invited from registered medical practitioners for the post of Full-time ASSISTANT MEDICAL OFFICER OF HEALTH AND SCHOOL MEDICAL OFFICER, with duties covering the whole range of local authority health and welfare services. Salary scale £1050–£1475. The post is superannuated, and subject to 2 months' notice on either side.

Applications should be made to the Town Clerk, Town Hall, West Bromwich, not later than 15th November, 1958, giving details of experience and the names of 3 referees.

AUSTRALIA. MENTAL HYGIENE AUTHORITY OF VICTORIA has vacancies for PSYCHIATRISTS experienced in :—
(*a*) Mental Hospital Psychiatry.
(*b*) Mental Deficiency Services and Child Psychiatry.
(*c*) Forensic Psychiatry.

Applicants must be qualified for registration by the Victoria Medical Board and hold a D.P.M., M.D. or M.R.C.P., with a minimum 3 years' experience after having gained postgraduate diploma or degree.

Annual salary £A3162 payable from date of embarkation. Good residences available on a rental basis. Superannuation also available if desired.

Transport Expenses.—A sum of £500 will be paid to appointee proceeding to Australia if he contracts to remain in the service for at least 3 years. (£250 in the case of single appointees.)

Further particulars obtainable from the Secretary, Mental Hygiene Authority, 300, Queen-street, Melbourne, Victoria, Australia.

EAST AFRICAN TRYPANOSOMIASIS RESEARCH ORGANISATION. MEDICAL RESEARCH OFFICER with registrable medical qualifications and aptitude for research required to undertake research on epidemiology of trypanosomiasis. Postgraduate research experience in the epidemiology of insect-borne diseases an advantage. Possible posting would be at Tororo, Uganda. Appointment can be on permanent basis or short-term agreement for a tour of 36 months with gratuity (taxable) of 13⅓% of salary. Salary scale £1284–£1863 p.a., starting-point determined by experience. Contributory superannuation scheme for candidates appointed on probation. Return passages provided for officer, wife, and dependent children under 21, up to cost of 3 adult sea passages or 4 adult air passages. Accommodation, including basic furniture for officer and family, available at low rental. Income-tax at Uganda rates. Generous home and local leave.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD.195/198/02).

GOVERNMENT OF THE FEDERATION OF NIGERIA. PATHOLOGISTS with medical degree registrable in United Kingdom and experience in a pathology department in United Kingdom or Eire required to carry out routine hæmatology, chemical pathology, and morbid anatomy, and to train laboratory technicians. Opportunities for individual research in clinical pathology. Higher qualification (e.g., D.C.P. or Dip. Bact.) an asset. Appointment either (*a*) on contract for 1 tour (approximately 18 months) in first instance with gratuity (taxable) of £37 10s. for each completed period of 3 months' satisfactory service; or (*b*) from National Health Service candidates retaining superannuation rights and receiving gratuity (taxable) of 20% of aggregate salary. Salaries under (*a*) in scale £1338–£2286 p.a., and (*b*) £1128–£1950 ; point of entry in both cases determined by age, experience and qualifications. In addition staff pay £100 a year is payable. Quarters with heavy furniture usually available at low rental. Return passages for officer and wife. Officer can claim actual amount expended in any 1 tour (up to cost of 2 adult return passages) for children under age 18 to join him in Nigeria, or for wife to visit them in home country. Children's (separate domicile) allowance of £75 a year for each of 2 children under 18, ceasing if child joins parents in Nigeria. Income-tax at local rates. Local leave permissible and generous home leave after tour.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD.117/14/05).

SASKATCHEWAN. DEPARTMENT OF PUBLIC HEALTH
requires for its
Physical Restoration Programme
Headquarters—Regina

DIRECTOR OF PHYSICAL MEDICINE File No. 5649
$9936–$12,084

Specialist in Physical Medicine with experience in practice of specialty and in administration ; to direct and develop an established rehabilitation programme within a rehabilitation centre of 50 inpatient beds and to assist in the promotion and development of physical medicine in general hospitals throughout the province.

SPECIALIST IN PHYSICAL MEDICINE File No. 5650
$9552–$11,616

To be responsible to the Director of Physical Medicine in an expanding rehabilitation centre of 50 inpatient beds and a large outpatient case-load with a staff of physiotherapists, occupational therapists, speech therapists, teacher therapists, psychologist, and social workers.

Forms and further information available at Public Service Commission, Legislative Building, or Personnel Officer, Department of Public Health, Provincial Health Building, Regina, Saskatchewan, Canada. Applicants should quote file numbers.

WEST AFRICAN INSTITUTE FOR TRYPANOSOMIASIS RESEARCH. MEDICAL RESEARCH OFFICER Grade 2 or 3, with medical degree registrable in United Kingdom and at least 2 years' postgraduate research experience, required to work under officer-in-charge of research on human trypanosomiasis. Experience in immunology, protozoology, and tissue culture an advantage. Appointment on contract for 1 tour of 18–24 months in first instance, with gratuity of £37 10s. for each completed period of 3 months' service payable on satisfactory completion of appointment. Salary (grade 3) £1248–£1434, (grade 2) £1482–£1770. Return passages for officer and wife. Officer can claim actual amount expended in any 1 tour (up to cost of 2 adult fares) for children under 18 years old to join him in Nigeria, or for wife to visit them in home country. Quarters with basic furniture available at low rental. Local income-tax. Local leave permissible and generous home leave after each tour. Children's (separate domicile) allowance of £75 a year for each child under 18 years old, ceasing if child joins parents in Nigeria. Outfit allowance £60.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD.197/198/012).

General Practice

For an Executive Council post (England and Wales) apply on form E.C.16A obtainable from the council. Mark envelope "Vacancy."

READING EXECUTIVE COUNCIL. Applications are invited from registered medical practitioners for VACANCY in Eastern Area of Borough. Classification—Intermediate. List as at 1st October—1143, including County patients. House, including surgery accommodation, available for sale, subject to negotiation with owner. Applications, on Form E.C.16A, to be received by the undersigned not later than first post on Thursday, 6th November, 1958. N. W. AUSTIN, Clerk of the Council.
10, Gun-street, Reading, Berks.

Miscellaneous

Industrial Medical Officer, full-time, required at Metropolitan-Vickers Electrical Co. Ltd., Trafford Park, Manchester, 17, commencing as soon as possible. Postgraduate, casualty, and general practice experience preferred. Industrial experience not required, enthusiasm essential. B.M.A. salary.—Apply in writing to the Chief Medical Officer, giving full particulars.

MSL have been retained to advise on the appointment of the

CHIEF MEDICAL ADVISER
TO
THE WELLCOME FOUNDATION LIMITED

The Chief Medical Adviser will be responsible to the Research Director for planning and directing the work of the Medical Research Department.

He will be required, with the assistance of his team of medically qualified staff, to arrange clinical investigations and evaluate the results, and to provide authoritative medical advice on established, new and prospective products. Collaboration with the company's sales divisions, as well as with its research laboratories, will be involved. He will also maintain close liaison with the medical departments of overseas subsidiary companies.

The status of the appointment is such that candidates must have had wide and varied clinical experience and be at least 40 years of age; a higher qualification would be an advantage. They should also have had sustained contact with the pharmaceutical industry, either by conducting clinical trials in collaboration with pharmaceutical firms or by holding an appointment within the industry.

No information will be disclosed to our clients until candidates have given permission after a personal and confidential discussion. Please send details of qualifications, experience and publications, in confidence, quoting reference AN.1262, to R. A. Denerley.

MANAGEMENT SELECTION LIMITED
17, Stratton Street, London, W.1

New York City. Leading child guidance agency has opening for Psychiatrist to direct new project in testing and developing child guidance techniques. 25–35 hours per week; analytic training and experience in treatment of children required. Approximate salary will be made available. Address inquiries: Address No. 435, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Harley House. Suitable for Doctor to live and practise. Constant hot water. Full porterage. 4 bedrooms, dining-room, living-room, 2 other rooms, kitchen, &c.—Apply for full details to sole agents, ELLIOTT, SON & BOYTON, 86/87, Wimpole-street, W.1 (WEL. 8367).

On Sussex Heights. Hotel premises suitable for institutional use. For sale freehold, with furnishings if required. The property stands in nearly 3 acres with valuable main road and subsidiary road frontages with planning permission for partial development. 40 bedrooms, 12 bathrooms. The hotel has been running for about 25 years and shows a very considerable turnover.—Details from the Sole Agents, BERNARD THORPE & PARTNERS, 129, Mount-street, Mayfair, W.1. Telephone: GROsvenor 2501. Westminster, Oxted, Hereford, York, Darlington, Newcastle, Hexham and Edinburgh.

Unfurnished Maisonette to let, 5 rooms, third and fourth floors, Harley-street. Used for practice and residence.—For appointment ring WEL. 2359.

"Pregnancy Diagnosis by the Xenopus Method," 24-hour service. Send specimens of urine and £2 2s. fee. Hæmatology, Biochemistry, Flame Photometry.—WELBECK BIOLOGICAL LABORATORIES, 26, Park-crescent, Portland-place, W.1 (MUSeum 5386–7).

Doctors requiring applications, theses copied: Write to MANTON (WESTMINSTER) LTD., 153, Victoria-street, S.W.1 (VIC. 0141), who are specialists.

Typewriting and Duplicating. First-class work at moderate prices by experienced medical typists. Electric machines. —SYBIL RANG, 21, Heath-street, Hampstead, London, N.W.3 (HAM 5329/0504).

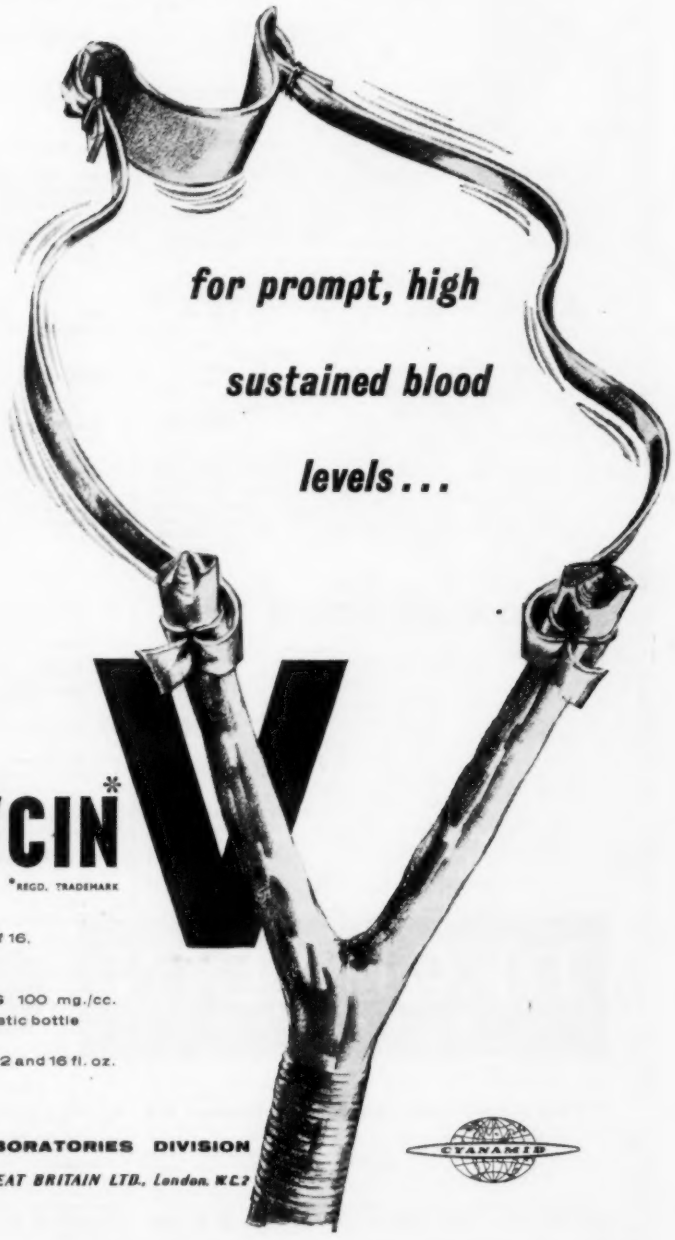
Old medical and scientific books, pictures, manuscript notebooks, letters, &c., wanted by a collector.—Address, No. 343, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Pregnancy Diagnosis (Fee 21s.). Specimens of urine accepted for testing (Hogben test) from doctors, hospitals and clinics anywhere. Results available within 24 hours. Fee reduced for hospitals and clinics. Telephone or write for details : FAMILY PLANNING ASSOCIATION, 64, Sloane-street, London, S.W.1. SLOane 0451 or 9112.

PUBLISHED by the PROPRIETORS, THE LANCET LIMITED, 7, Adam Street, Adelphi, in the County of London.
Printed by HAZELL, WATSON AND VINEY, LTD., Leigh Road, Slough and Aylesbury—Saturday, November 1, 1958.
PRINTED IN GREAT BRITAIN—Entered as Second Class at the New York, U.S.A., Office.

CATAPULTED

into high favour



for prompt, high sustained blood levels...

ACHROMYCIN* V

BUFFERED TETRACYCLINE *REGD. TRADEMARK

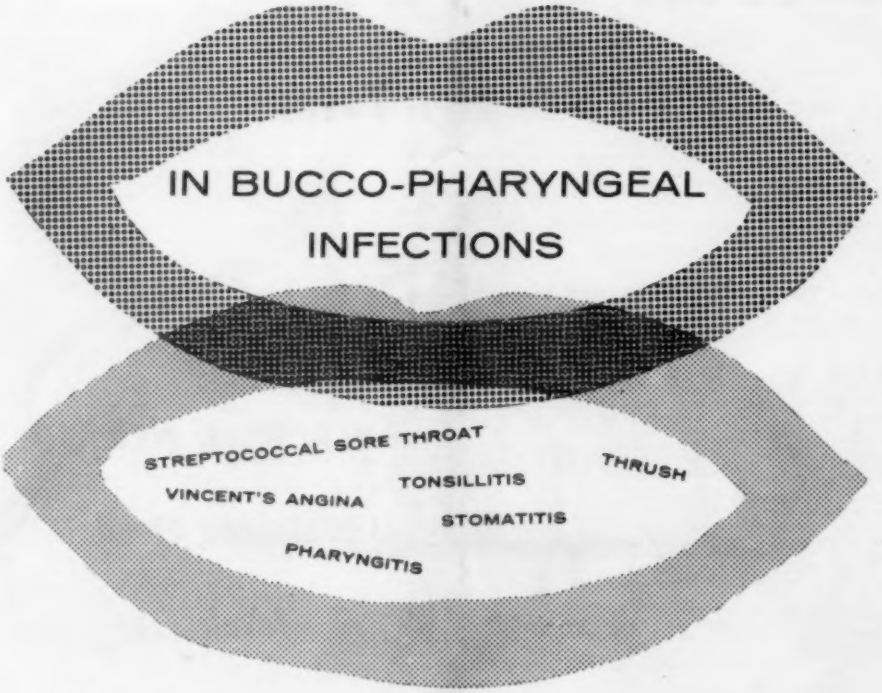
CAPSULES 250 mg. Bottles of 16, 100 and 1000.

PEDIATRIC DROPS AQUEOUS 100 mg./cc. 1 Gm. in 10 cc. Plastic bottle

SYRUP 125 mg./5 cc. Bottles of 2 and 16 fl. oz.

Lederle LEDERLE LABORATORIES DIVISION
Cyanamid OF GREAT BRITAIN LTD., London, W.C.2

CYANAMID



DEQUADIN

- rapidly and effectively controls the infection
- avoids the risks involved in local antibiotic therapy
- is more widely effective against oral pathogens than penicillin
- is fully active in the presence of serum
- is completely non-toxic

DEQUADIN LOZENGES

Available as DEQUADIN LOZENGES, in tubes of 20 lozenges.

Dosage: One lozenge sucked slowly every 2 or 3 hours.

STANDARD REFERENCE CARD ON APPLICATION

Manufactured in England by ALLEN & HANBURYS LTD LONDON E2

N 58 112 H